Appendices Guideline Safe Use of Contrast Media - Part 1

Appendices to Chapter 4

Author and year	Ill text (initial search): Risk factors for PC-AKI Reasons to exclude
Abe, 2011	Does not meet selection criteria
Abujudeh, 2008	Examines risk of PC-AKI in patients who underwent 2 CT-scans within 24 hours
, ibajaacii, 2000	not applicable for overall recommendations
Acosta, 2010	Does not meet selection criteria
Agrawal, 2009	Does not meet selection criteria
Aguiar-Suato, 2010	Does not meet selection criteria
Ahuja, 2010	Does not meet selection criteria
Akgullu, 2015	Does not meet selection criteria
Akrawinthawong, 2015	Does not meet selection criteria
Alharazy, 2013	Does not meet selection criteria
Bachorzewska-Gajewska, 2006	Does not meet selection criteria
Balemans, 2012	Does not meet selection criteria
Band, 2007	Does not meet selection criteria
Barbieri, 2014	Does not meet selection criteria
Becker, 2006	Does not meet selection criteria
Canyigit, 2013	Does not meet selection criteria
Caruso, 2011	Does not meet selection criteria
Cely, 2012	Does not meet selection criteria
Chang, 2013	Studies gene polymorphisms and their relation to PC-AKI risk; not applicable in
	common Dutch clinical practice.
Chavakula, 2013	Does not meet selection criteria
Chen, 2014	Does not meet selection criteria
Cho, 2011	Does not meet selection criteria
Chong, 2009	Does not meet selection criteria
Chong, 2010_1	Does not meet selection criteria
Chong, 2010_2	Does not meet selection criteria
Chong, 2012	Does not meet selection criteria
Cheruvu, 2007	Does not meet selection criteria
Crit, 2006	Does not meet selection criteria
Clark, 2011	Does not meet selection criteria
Clec'h, 2013	Does not meet selection criteria
Colling, 2014	Does not meet selection criteria
Conen, 2006	Does not meet selection criteria
Cowburn, 2005	Does not meet selection criteria
Dangas, 2005	Does not meet selection criteria
Davidson, 2008	Does not meet selection criteria
Ding, 2013	Does not meet selection criteria
Diogo, 2010	Does not meet selection criteria
Diogo, 2014	Does not meet selection criteria
Dittrich, 2006	Does not meet selection criteria
Dittrich, 2007	Does not meet selection criteria
Durukan, 2012	Does not meet selection criteria
Elias, 2005	Does not meet selection criteria
Erdogan, 2003	Does not meet selection criteria
Erselcan, 2012	Does not meet selection criteria
Friedewald, 2013	Does not meet selection criteria
From, 2008	Does not meet selection criteria
Fu, 2013	Does not meet selection criteria
Gao, 2011	Does not meet selection criteria
Gao, 2014	Does not meet selection criteria
Garcia, 2014	Does not meet selection criteria
Garcia-Ruiz, 2003	Does not show multivariate model that predicts risk factors of PC-AKI

Calchabi 2014	Does not most selection criteria						
Golshahi, 2014	Does not meet selection criteria						
Goo, 2014	Does not meet selection criteria						
Guevara, 2004	Does not meet selection criteria						
Gurm, 2011	Does not meet selection criteria						
Grum, 2013	Does not meet selection criteria						
Hassen, 2014	Does not meet selection criteria						
Haveman, 2006	Does not meet selection criteria						
Hayakawa, 2014	Patient population: patients with hepatocellular carcinoma undergoing trans-						
	arterial chemo-embolization. Article too specific to draw overall conclusions						
	over intra-arterial contrast administration and risk of PC-AKI.						
Hernández, 2009	Already included in systematic review Bondi-Zoccai, 2014						
Hipp, 2008	Does not meet selection criteria						
Holscher, 2008	Does not meet selection criteria						
Hoste, 2011	Does not meet selection criteria						
Huang, 2013	Does not meet selection criteria						
Huggins, 2014	Does not meet selection criteria						
Ivanes, 2014	Does not meet selection criteria						
Jaipaul, 2010	Does not meet selection criteria						
Jarai, 2012	Does not meet selection criteria						
Ji, 2015	Does not meet selection criteria						
Jochheim, 2014	Does not meet selection criteria						
Jo, 2015	Does not meet selection criteria						
Kato, 2008	Does not meet selection criteria						
Kian, 2006	Does not meet selection criteria						
Kim, 2011	Does not meet selection criteria						
Kim, 2012	Does not meet selection criteria						
Kim, 2012	Does not meet selection criteria						
Kiski, 2009	Does not meet selection criteria						
Kiski, 2009	Does not meet selection criteria						
Koo, 2013	Does not meet selection criteria						
Kougias, 2014	Does not meet selection criteria						
Kuhn, 2008	Does not meet selection criteria						
Kwasa, 2014	Does not meet selection criteria						
Lameire, 2006	Does not meet selection criteria						
Laskey,2009	Does not meet selection criteria						
Lee, 2014	Does not meet selection criteria						
Lencioni, 2010	Does not meet selection criteria						
Leung, 2014	Model predicts use of cardiac medication after development of PC-AKI, but						
	does not predict risk of PC-AKI						
Li, 2013	Does not meet selection criteria						
Li, 2014	Does not meet selection criteria						
Liebetrau, 2014	Does not meet selection criteria						
Limbruno, 2014	Does not meet selection criteria						
Lin, 2014	Does not meet selection criteria						
Liu, 2012_1	Does not meet selection criteria						
Liu, 2012_2	Does not meet selection criteria						
Liu, 2013	Does not meet selection criteria						
Liu, 2014	Does not meet selection criteria						
Lodhia, 2009	Does not meet selection criteria						
Lucreziotti, 2014	Does not meet selection criteria						
Lui, 2012	Does not meet selection criteria						
Macaulay, 2015	Does not answer research question, no multivariate analysis performed (n=7)						
Madershahian, 2012	Does not meet selection criteria						
Madershahian, 2012	Does not meet selection criteria						
Madsen, 2009	Does not meet selection criteria						
Mager, 2011	Does not meet selection criteria						
Maioli, 2010	Does not meet selection criteria						
Maioli, 2012	Does not meet selection criteria						
Malyszko, 2009	Does not meet selection criteria						
Marenzi, 2004_1	Does not meet selection criteria						
THUI CITE, 2004_1							

Marenzi, 2004_2	Does not meet selection criteria
Matsushima, 2011	Does not meet selection criteria
McCullough, 2006_1	Does not meet selection criteria
McCullough, 2006_2	Does not meet selection criteria
McDonald, 2014_1	Does not meet selection criteria
McDonald, 2014_2	Does not meet selection criteria
Medalion, 2010	Does not meet selection criteria
Mehran, 2004	Does not meet selection criteria
Mehran, 2009	Does not meet selection criteria
Mehta, 2004	Does not meet selection criteria
Mekan, 2004	Does not meet selection criteria
Moos, 2013	Does not meet selection criteria
Moos, 2014	Does not show multivariate model that predicts risk factors of PC-AKI (but
	tests existing models)
Morabito, 2012	Does not meet selection criteria
Morcos, 2012	Does not meet selection criteria
Murakami, 2013	Does not meet selection criteria
Najjar (ea) 2002	Does not meet selection criteria
Naruse, 2012	Does not meet selection criteria
Ng, 2010	Does not meet selection criteria
Nikolsky, 2004	Does not meet selection criteria
Nikolsky, 2005	Does not meet selection criteria
Nozue, 2009	Does not meet selection criteria
Nyman, 2005	Does not meet selection criteria
Onuigbo, 2008	Does not meet selection criteria
Osman, 2014	Does not meet selection criteria
Owen, 2014	Does not meet selection criteria
Padhy, 2014	Does not meet selection criteria
Pahade, 2011	Does not meet selection criteria
Pakfetrat, 2010_1	Does not meet selection criteria
Pakfetrat, 2010 2	Does not meet selection criteria
Parra, 2004	Does not meet selection criteria
Patel, 2010	Review, not systematic and does not answer research question
Peguero, 2014	Does not meet selection criteria
Peng, 2015	Does not meet selection criteria
Piskinpasa, 2013	Combination of CAG and CT-scan patients (n=70), not analysed separately.
Polena, 2005	Does not meet selection criteria
Prasad, 2014	No multivariate analysis of risk factors for PC-AKI was performed
Rahman, 2005	Does not meet selection criteria
Raingruber, 2011	Does not meet selection criteria
Ranucci, 2013	Does not meet selection criteria
Raposeiras, 2015	Does not meet selection criteria
Raposeiras, 2015	Does not meet selection criteria
Ray, 2013	Does not meet selection criteria
Reuter, 2014	No multivariate analysis of risk factors for PC-AKI was performed
Sahin, 2014	Does not meet selection criteria
Saito, 2015	Does not meet selection criteria
Saritemur, 2014	Does not meet selection criteria
Sendur, 2013	Does not meet selection criteria
Sharma, 2013	Does not meet selection criteria
Shema, 2009	Does not meet selection criteria
Sidhu, 2008	Does not meet selection criteria
Skelding, 2007	Does not answer research question, validation of risk score
Spatz, 2012	Does not meet selection criteria
Spini, 2013	Does not meet selection criteria
Spini, 2013 Standstede, 2007	Does not meet selection criteria
· ·	
Stermer, 2001	Does not meet selection criteria
Subedi, 2011	Does not meet selection criteria
Tan, 2013	Does not meet selection criteria
Taniguchi, 2013	Does not meet selection criteria

Thomsen, 2003	Does not meet selection criteria				
Thomsen, 2009	Does not meet selection criteria				
Toprak, 2006_1	Does not meet selection criteria				
Toprak, 2006_2	Does not meet selection criteria				
Toprak, 2007	Does not meet selection criteria				
Trivedi, 2010	Does not meet selection criteria				
Tziakas, 2014	Does not meet selection criteria				
Ucar, 2014	Does not meet selection criteria				
Ugur, 2014	Does not meet selection criteria				
Umruddin, 2012	Does not meet selection criteria				
Utsunomiyama, 2011	Studies risk factors for kidney insufficiency, not risk factors for development of				
	PC-AKI after CT-scan				
Victor, 2014	Does not meet selection criteria				
Wacker-Gusmann, 2014	Does not meet selection criteria				
Wang, 2011	Does not meet selection criteria				
Weisbord, 2006	Does not meet selection criteria				
Wessely, 2009	Does not meet selection criteria				
Wi, 2013	Does not meet selection criteria				
Yamamoto, 2013	Does not meet selection criteria				
Zaytseva, 2009	Does not meet selection criteria				

Exclusion after examination of full text (update 2017): Risk factors for PC-AKI

Author and year	Redenen van exclusie
Kanda, 2016	Does not meet selection criteria
Prasad, 2016.	Does not meet selection criteria
Abouzeid, 2016	Does not meet selection criteria
Agarwal, 201	Does not meet selection criteria
Azzalini, 2016	Does not meet selection criteria
Cernigliaro, 2016	Does not meet selection criteria
Briguori, 2016	Does not meet selection criteria
Chong, 2015	Does not meet selection criteria
de Francesco, 2015	Does not meet selection criteria
Dong, 2016	Does not meet selection criteria
Filomia 2016	Does not meet selection criteria
Guneyli, 2015	Does not meet selection criteria
Gurm, 2016.	Does not meet selection criteria
Subramaniam, 2016	Does not meet selection criteria
Ye, 2016 / Ye, 2017	Does not meet selection criteria
Zapata-Chica, 2015	Does not meet selection criteria
Hinson, 2017	Does not meet selection criteria
Hong, 2016	Does not meet selection criteria
Hsieh, 2016	Does not meet selection criteria
Huber, 2016	Does not meet selection criteria
Kanbay, 2017,	Does not meet selection criteria
Khaledifar, 2015	Does not meet selection criteria
Kim, 2015	Does not meet selection criteria
Komiyama, 2017	Does not meet selection criteria
Liu 2015	Does not meet selection criteria
McDonald 2015	Does not meet selection criteria
Nijssen, 2017	Does not meet selection criteria
Nyman, 2015	Does not meet selection criteria
Ortega, 2015	Does not meet selection criteria
Park, 2016	Does not meet selection criteria
Sato, 2015	Does not meet selection criteria
Shema, 2016	Does not meet selection criteria
Sigterman, 2016	Does not meet selection criteria
Salomon, 2015	Does not meet selection criteria
Tong, 2016,	Does not meet selection criteria
Turedi, 2016	Does not meet selection criteria
Usmiani, 2016	Does not meet selection criteria

Valette, 2017	Does not meet selection criteria
Vontobel, 2015	Does not meet selection criteria
Winther, 2016	Does not meet selection criteria
Xu, 2016	Does not meet selection criteria
Yang, 2014	Does not meet selection criteria
Zeller, 2016	Does not meet selection criteria

Exclusion after examination of full tekst: Measurement instruments for PC-AKI risk

Author and year	Reasons for exclusion							
Aguiar, 2008	Letter to the editor							
Akgullu, 2015	Does not fulfill selection criteria, no risk score is validated/developed							
Balemans, 2012	Does not fulfill selection criteria, no risk score is validated/developed							
Bartholemew, 2004	Already included in systematic review Silver, 2015							
Benko, 2007	Not an original article (guideline)							
Celik, 2015	The diagnostic properties of a laboratory analysis (contrast media volume toe							
Celik, 2015	GFR ratio) to predict PC-AKI are examined, not of a non-invasive method.							
Chen, 2014	Already included in systematic review Silver, 2015							
Chong, 2012	Does not fulfill selection criteria, no risk score is validated/developed							
Crit, 2006	Does not fulfill selection criteria, no risk score is validated/developed							
Davenport, 2013	The diagnostic properties of a laboratory analysis (different eGFR cut-off							
• •	values) to predict PC-AKI are examined, not of a non-invasive method.							
Davenport, 2013_1	The diagnostic properties of a laboratory analysis (different eGFR cut-off							
	values) to predict PC-AKI are examined, not of a non-invasive method							
Erselcan, 2009	The diagnostic properties of a laboratory analysis (eGFR by MDRD formula) to predict PC-AKI are examined, not of a non-invasive method.							
Feldkamp, 2008	Narrative review							
Fu, 2013	Already included in systematic review Silver, 2015							
Gao, 2014	Already included in systematic review Silver, 2015							
Ghani, 2009	Already included in systematic review Silver, 2015							
Gurm, 2013	Already included in systematic review Silver, 2015							
Holscher, 2008	Does not fulfill selection criteria, no risk score is validated/developed							
Kim, 2011								
Kin, 2011 Kooiman, 2010	Does not fulfill selection criteria, no risk score is validated/developed							
· · ·	Does not fulfill selection criteria, no risk score is validated/developed							
Kowalczyk, 2007	Does not fulfill selection criteria, no risk score is validated/developed							
Lepanto, 2011	Narrative review							
Li, 2013	The diagnostic properties of a laboratory analysis (anemia) to predict PC-AKI are examined, not of a non-invasive method.							
Liu, 2014	Already included in systematic review Silver, 2015							
Maioli, 2011	Already included in systematic review Silver, 2015							
Marenzi, 2004	Already included in systematic review Silver, 2015							
Martainez – Lomakin, 2014	The diagnostic properties of a laboratory analysis (point of care creatinin test)							
	to predict PC-AKI are examined, not of a non-invasive method.							
McCullough, 2001	Narrative review							
McCullough, 2007	Narrative review							
McDonald, 2014	Does not fulfill selection criteria, no risk score is validated/developed							
Mehran, 2004	Already included in systematic review Silver, 2015							
Owen, 2014	Not an original article (guideline)							
Pakfetrat, 2010	Does not fulfill selection criteria, no risk score is validated/developed							
Rainburger, 2011	PC-AKI is not an outcome measure.							
Saito, 2015	The diagnostic properties of a laboratory analysis (proteinuria and to predict							
0.0010	PC-AKI are examined, not of a non-invasive method.							
Sany, 2013	Does not meet selection criteria, no risk score is validated/developed							
Skelding, 2007	Does not fulfill selection criteria, pre-defined outcome variables not reported							
Skluzacek, 2003	The diagnostic properties of a laboratory analysis (eGFR) to predict PC-AKI are							
T 4000	examined, not of a non-invasive method.							
Tong, 1996	The diagnostic properties of a laboratory analysis (neutrophil gelatinase associated lipoprotein) to predict PC-AKI are examined, not of a non-invasive							
	method.							
Тоо, 2015	PC-AKI is not an outcome measure. The questionnaire's ability to predict eGFR is examined.							

Tziakas, 2013	Already included in systematic review Silver, 2015					
Wackecker-Gußmann, 2014	The diagnostic properties of a laboratory analysis (cystatin C) to predict PC-AKI					
	are examined, not of a non-invasive method.					
Wang, 2011	The diagnostic properties of a laboratory analysis (contrast media volume toe					
	GFR ratio) to predict PC-AKI are examined, not of a non-invasive method.					
Worasuwannarack, 2011	Article not found (Taiwanese journal)					
Zahringer, 2014	PC-AKI is not an outcome measure. The questionnaire's ability to predict eGFR					
	is examined.					

Exclusion after examination of full text (update 2017): Measurement instruments for PC-AKI risk

Author and year	Reasons for exclusion
Akrawinthawong, 2015	Does not meet selection criteria
Ando, 2013	Does not meet selection criteria
Anonymous, 2015	Erratum
Balli, 2016	Does not meet selection criteria
Barbieri, 2016	Does not meet selection criteria
Chatterjee, 2017	Does not meet selection criteria
Garfinkle, 2015	Does not meet selection criteria
Goussot, 2015	Does not meet selection criteria
Grossman, 2017	Does not meet selection criteria
Gurm, 2016	Does not meet selection criteria
Hsieh, 2016	Does not meet selection criteria
Kim, 2015	Does not meet selection criteria
Li, 2016	Does not meet selection criteria
Liu, 2015	Does not meet selection criteria
Oksuz, 2015	Does not meet selection criteria
Osugi, 2016	Does not meet selection criteria
Ozturk, 2016	Does not meet selection criteria
Park, 2017	Does not meet selection criteria
Prasad, 2016	Does not meet selection criteria
Raposeiras-Roubin, 2013	Does not meet selection criteria
Sato, 2015	Does not meet selection criteria
Тао, 2016	Does not meet selection criteria
Victor, 2014	Does not meet selection criteria
Watanabe, 2016	Does not meet selection criteria
Xu, 2016	Does not meet selection criteria
Yin, 2017	Does not meet selection criteria
Yuan, 2017	Does not meet selection criteria
Brown, 2015	Does not meet selection criteria

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate	Comprehensive	Description of	Description of	Appropriate adjustment for	Assessment of	Enough	Potential risk	Potential
	and clearly	and systematic	included and	relevant	potential confounders in	scientific	similarities	of publication	conflicts of
	focused	literature	excluded	characteristics	observational studies? ⁵	quality of	between	bias taken into	interest
	question? ¹	search? ²	studies? ³	of included		included	studies to	account? ⁸	reported? ⁹
				studies? ⁴		studies? ⁶	make		
							combining		
							them		
First							reasonable? ⁷		
author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Eng, 2016	Yes	Yes	No	Yes	Yes	No	Yes	No	No

1. Research question (PICO) and inclusion criteria should be appropriate and predefined

2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched

3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons

4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported

5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)

6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)

7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I²)?

8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials) Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year)		(unlikely/likely/unc lear)	(unlikely/likely/uncl ear)	(unlikely/likely/ unclear)	(unlikely/likely/uncl ear)	(unlikely/likely/ unclear)	(unlikely/likely/un clear)	(unlikely/likely/uncle ar)
Chen, 2007	Not described "patients were randomly allocated"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Jurado- Roman, 2014	Not described "patients were randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Kooiman, 2014	Computer generated allocation sequence	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Maioli, 2011	Computer generated, open- label randomization block	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Risk of bias table for intervention studies (observational: non-randomized clinical trials, cohort and case-control studies) Research question:

Study reference	Bias due to a non-representative or ill- defined sample of patients? ¹	Bias due to insufficiently long, or incomplete follow-up, or differences in follow-up between treatment groups? ²	Bias due to ill-defined or inadequately measured outcome ? ³	Bias due to inadequate adjustment for all important prognostic factors? ⁴
(first author, year of				
publication)	(unlikely/likely/unclear)	(unlikely/likely/unclear)	(unlikely/likely/unclear)	(unlikely/likely/unclear)
Bruce, 2009	Unlikely	Unclear	Unlikely	Likely
Davenport, 2013	Unlikely	Unclear	Unlikely	Likely
McDonald, 2013	Unlikely	Unclear	Unlikely	Likely

1. Failure to develop and apply appropriate eligibility criteria: a) case-control study: under- or over-matching in case-control studies; b) cohort study: selection of exposed and unexposed from different populations.

2. 2 Bias is likely if: the percentage of patients lost to follow-up is large; or differs between treatment groups; or the reasons for loss to follow-up differ between treatment groups; or length of follow-up differs between treatment groups or is too short. The risk of bias is unclear if: the number of patients lost to follow-up; or the reasons why, are not reported.

- 3. Flawed measurement, or differences in measurement of outcome in treatment and control group; bias may also result from a lack of blinding of those assessing outcomes (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Failure to adequately measure all known prognostic factors and/or failure to adequately adjust for these factors in multivariate statistical analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient	Intervention (I)	Comparison / control	Follow-up	Outcome measures and	Comments		
reference	characteristics	characteristics		(C)		effect size			
Eng, 2016	SR and meta-	Inclusion criteria	Describe intervention:	Describe control:	End-point of follow-up:	Outcome measure-1	Facultative:		
	analysis of RCTs	SR:			72 hours	Defined as CIN			
[individua		1) RCTs that	LOCM contrast	Iodixanol contrast			Brief description of		
l study	Literature search	compared	administration	administration		Intra-arterial contrast	author's conclusion		
characteri	up to June 2015	LOCM to IOCM			For how many	administration			
stics		with CIn	Both ia and iv	Both ia and iv	participants were no	Favors iodixanol:	No differences were		
deduced	Study design:	incidence as the			complete outcome data	Relative risk (RR): 0.80	found in CIN risk among		
from [1st	RCT [parallel]	main outcome			available?	(0.64 - 1.01)	types of LOCM. Iodixanol		

author		as the main		(intervention (control)	$1^{2}-42\%$ = -0.02	had a slightly lower risk
author,	Catting and			(intervention/control)	l ² =43%, p=0.03)	had a slightly lower risk
year of	Setting and	outcome in		Not described		for CIN than LOCM, but
publicatio	Country: United	patients having			Intra-venous contrast	the lower risk did not
n]	States of	diagnostic			administration	exceed the criterium for
	America	imaging or			Favors iodixanol:	clinical importance.
PS., study		image-based			Relative risk (RR): 0.84	
characteri	Source of	therapeutic			(0.42 – 1.71)	Level of evidence: GRADE
stics and	funding: non-	procedures			l ² =29%, p=0.22)	(per comparison and
results	commercial	2) CIN incidence				outcome measure)
are		is based on sCr				including reasons for
extracted		or eGFR at				down/upgrading
from the		baseline and				
SR (unless		within 72 hours				Most of the included
stated		of injection				studies GRADEd as Low
otherwise						(due to imprecision)
)		Exclusion				
•		criteria SR:				
		1) language				
		other than				
		English				
		2) mixed route				
		of contrast				
		administration				
		daministration				
		29 studies				
		included				
		mended				
		Groups				
		comparable at				
		baseline?				
		Unclear	l	l		

AKI: acute kidney injury; CI-AKI: contrast induced acute kidney injury; CIN: contrast induced nephropathy; CT: Computed Tomography; eGFR: estimated glomerular filtration ration; ia: intra-arterial; IOCM: iso-osmolar contrast medium; iv: intravenous; LOCM: low osmolair contrast medium; RCT: randomized controlled trial; sCr: serum creatinine;

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])¹ This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study	Study	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures	Comments
reference	characteristics					and effect size ⁴	
	1	· · · · · · · · · · · · · · · · · · ·	rast administration versus no co		017	1	1
Bruce,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2009	retrospective	1) age at least 18	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
	observational	years,			3 days	(include 95%CI and p-	We identified a high
		measurement of				value if available):	incidence of acute
	Setting: in-	serum creatinine	administration of	Unenchanced Computed	Loss-to-follow-up:		kidney injury among
	and	concentration within 30	isoosmolarcontrast medium	Tomography	Unclear, only	Acute kidney injury	control subjects
	outpatients,	days before CT, and	(IOCM) (iodixanol) prior to		patients that had	(=a 0.5 mg/dL	undergoing
	multicentre	creatinine measurement	Computed Tomography (CT)		a creatinine	increase in serum	unenhanced CT. The
	study	with result available			measurement at	creatinine	incidence of
		within 3 days after the			baseline and after	concentration or a	creatinine elevation
	Country:	CT examination			3 days were	25% or greater	in this group was
	United States				included in this	decrease in estimated	statistically similar to
	of America	Exclusion criteria:			retrospective	glomerular filtration	that in the
		 patient received 			study.	rate within 3 days	isoosmolar contrast
	Source of	iodinated contrast				after CT)	medium group for all
	funding: not	material as part of			<u>Incomplete</u>		baseline creatinine
	reported	another procedure (e.g.,			outcome data:	In all groups, the	values and all stages
		cardiac catheterization)			As above	incidence of acute	of chronic kidney
		within 30 days before or				kidney injury	disease. These
		3 days after the				increased with	findings suggest that
		reference CT				increasing baseline	the additional risk of
		examination.				creatinine	acute kidney injury
		patients with a				concentration. No	accompanying
		preexisting status of				significant difference	administration of
		undergoing long-term				in incidence of	contrast medium
		Dialysis				presumed contrast-	(contrast-induced
		any record of dialysis				induced kidney injury	nephrotoxicity) may
		within				was identified	be overstated and
		30 days before or on the				between the	that much of the

r		· · · · ·		· · · · · · · · · · · · · · · · · · ·
	day of the CT		isoosmolar contrast	creatinine elevation
	examination		medium and the	in these patients is
			control groups. The	attributable to
	N total at baseline:		incidence of acute	background
	Intervention: 337		kidney injury in the	fluctuation,
	Control: 6815		low-osmolar contrast	underlying disease,
			medium cohort	or treatment.
	Important prognostic		paralleled that of the	
	factors ² :		control cohort up to a	Only patients that
	For example		creatinine level of 1.8	had a creatinine
	age ± SD:		mg/dL, but increases	measurement at
	<i>l:</i> 63 ± 16		above this level were	baseline and after 3
	<i>C: 59 ± 19</i>		associated with a	days were included in
			higher incidence of	this retrospective
	Sex:		acute kidney injury.	study.
	I: 65% M		, , , ,	
	C: 53% M			IV administration of
				low-osmolar contrast
	Groups comparable at			medium (LOCM)
	baseline? Yes			(iohexol) to patients
				with a
				documented serum
				creatinine
				concentration of
				2.0mg/dL or less if
				they did not have
				diabetes and to
				patients with a
				serum creatinine
				concentration of
				1.5 mg/dL if they did
				have diabetes. We
				added a high-risk
				tier, allowing
				administration of iso-
				osmolar contrast
				medium (IOCM)

							(iodixanol) to nondiabetic patients with baseline creatinine values up to a maximum of 2.5 mg/dL and to diabetic patients with values up to a maximum of 2.0 mg/dL. Estimated GFR values are currently computed for all outpatients but have not supplanted serum creatinine concentration for contrast administration decisions.
Davenport,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2013	retrospective	1) CT studies performed	(treatment/procedure/test):	(treatment/procedure/test):	up:	and effect size	
	observational	in patients who had never			72 hours	(include 95%Cl and p-	Intravenous LOCM is
	Setting: in-	undergone renal	contrast-enhanced CT	CT examinations without	Loss-to-follow-up:	value if available):	a nephrotoxic risk factor in patients
	and	replacement therapy	examinations	contrast enhancement	Early post- CT SCr	Post CT-AKI	with a stable eGFR
	outpatients,	(eg, dialysis, renal	with LOCM		data were	(= difference between	less than 30
	multicentre	transplantation),			available for	baseline and pre-CT	mL/min/1.73 m2,
	study	2) patients had available			1) 15 724 of 17	SCr within 0.3 mg/dL	with a trend
		data to permit			652 patients	and 50% of baseline)	Toward significance
	Country:	calculation of			(89.1%) 0–24	IV LOCM had a	at 30–44
	United States	the four-variable			hours after CT	significant effect on	mL/min/1.73 m ² . IV
	of America	Modification of Diet in Renal Disease formula			(7882 nonenhanced,	the development of post-CT AKI (<i>P</i> = .04).	LOCM does not appear to be a
	Source of	for eGFR,			7842 contrast-	μ USI-CI AKI ($P = .04$).	nephrotoxic risk
	funding: not	3) patients had all of the			enhanced),	This risk increased	factor in patients

reported	following SCr	2) 12 941 of 17	with decreases in pre-	with a pre-CT eGFR
	measurements	652	CT eGFR (>60 mL/	of 45 mL/min/1.73
	available:	patients (73.3%)	min/1.73 m ² :	m ² or greater.
	(a) baseline SCr (the	25–48 hours after	odds ratio, 1.00; 95%	
	most recent SCr	СТ	confidence interval:	
	obtained more than 5	(6450	0.86, 1.16;	
	days before the index	nonenhanced,	45–59 mL/min/1.73	
	СТ);	6491 contrast-	m ² :	
	(b) pre-CT SCr (the most	enhanced),	odds ratio, 1.06; 95%	
	recent SCr obtained	3) 10 213 of 17	confidence interval:	
	between the time of the	652 patients	0.82, 1.38;	
	index CT and 5 days	(57.9%) 49–72	30–44 mL/min/1.73	
	before);	hours after CT	m ² :	
	(c) at least one of	(5091	odds ratio, 1.40; 95%	
	three early post-CT SCr	nonenhanced,	confidence interval:	
	values (the first SCr	5122 contrast-	1.00, 1.97;	
	obtained in each 24-	enhanced).	<30 mL/min/1.73 m2:	
	hour period for the first		odds ratio, 2.96; 95%	
	72 hours after the index	<u>Incomplete</u>	confidence interval:	
	СТ).	outcome data:	1.22, 7.17)	
		As described		
	Exclusion criteria:	above		
	1) CT performed in a			
	patient who had an			
	earlier CT examination			
	that met			
	the inclusion criteria			
	2) missing data			
	regarding contrast			
	material administration			
	3) unstable renal			
	function before the CT			
	study			
	4) calculated eGFR was			
	greater than 200			
	mL/min/1.73 m ²			
	5) patients lacked a 1:1			

		propensity-matched					
		control					
		N total at baseline:					
		Intervention: 8826					
		Control: 8826					
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		1: 59 ± 17					
		C: 59 ± 18					
		Sex:					
		I: 48% M					
		C: 48% M					
		C. 4070 W					
		Groups comparable at					
		baseline? Yes					
McDonald,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2014	retrospective	1) all patients who	(treatment/procedure/test):	(treatment/procedure/test):	up:	and effect size	
	observational	underwent an			72 hours	(include 95%CI and p-	Following adjustment
		unenhanced	contrast-enhanced CT	CT examinations without		value if available):	for presumed risk
	Setting: in-	(noncontrast group) or	examinations	contrast enhancement	Loss-to-follow-up:		factors, the incidence
	and	intravenous			Unclear, only	CIN	of CIN was not
	outpatients,	contrastenhanced	Scan recipients were	Scan recipients were	patients that had	(=SCr ≥0.5 mg/dL	significantly different
	multicentre	(contrast group)	stratified with respect	stratified with respect	a creatinine	above baseline)	from contrast
	study	abdominal, pelvic,	to their presumptive risk for	to their presumptive risk for	measurement at		material-
		and/or thoracic CT scan	AKI by baseline SCr level as	AKI by baseline SCr level as	baseline and after	AKI risk was not	independent AKI.
	Country:	from January 1, 2000, to	follows:	follows:	3 days were	significantly different	These two
	United States	December 31, 2010, at	1) low risk, SCr ,<1.5 mg/dL;	1) low risk, SCr ,<1.5 mg/dL;	included in this	between contrast and	phenomena were
	of America	our institution;	2) medium risk, SCr 1.5–2.0	2) medium risk, SCr 1.5–2.0	retrospective	noncontrast groups in	clinically
	Source of	2) who had one or more postscan SCr results	mg/dL; 3) high risk, SCr >	mg/dL; 3) high risk, SCr >	study.	any risk subgroup after propensity score	indistinguishable with established SCr-
	funding: not	during the time period	2.0 mg/dL.	2.0 mg/dL.	Incomplete	adjustment by using	defined criteria,
	reported	of expected	2.0 mg/uL.	2.0 mg/uL.	outcome data:	reported risk factors	suggesting that
	reported	oi expected			outcome uata.		SUERESTINE LIIGT

development of CIN	As	above	of CIN	intravenous
(24–72 hours after CT-			1) low risk:	iodinated contrast
scanning)			odds ratio [OR], 0.93;	media may not be
3) who also had at least			95% confidence	the causative agent
one baseline SCr result			interval [CI]:	in diminished renal
in the 24-hour window			0.76,1.13; <i>P</i> = .47; 2)	function after
prior to scanning			medium risk: odds	contrast material
			ratio, 0.97; 95% CI:	administration.
Exclusion criteria:			0.81,	
1) patients who had			1.16; <i>P</i> = .76;	
preexisting renal dialysis			3) high risk: OR, 0.91;	
requirements;			95% CI: 0.66, 1.24;	
2) did not have			<i>P</i> = .58).	
sufficient SCr data to				
permit detection of AKI;			Counterfactual	
3) patients who			analysis revealed no	
underwent multiple			significant difference	
distinct CT-scans or			in AKI incidence	
percutaneous cardiac			between enhanced	
interventions with			and unenhanced CT	
iodinated contrast			scans in the same	
material within a 14-day			patient (McNemar	
period			test: x2 =0.63,	
			P = 0.43) (OR = 0.92;	
N total at baseline:			95% CI: 0.75, 1.13; P =	
Intervention: 10686			.46).	
Control: 10686				
Important prognostic				
factors ² :				
For example				
age (range):				
<i>l:</i>				
Low risk: 62 (49-74)				
Medium risk: 71 (59-79)				
High risk: 69 (58-77)				
C:				

		Low risk: 63 (48-74)					
		Medium risk: 71 (59-80)					
		High risk: 68 (56-77)					
		Sex:					
		I: % M					
		Low risk: 48%					
		Medium risk: 65%					
		High risk: 63%					
		C: % M					
		Low risk: 49%					
		Medium risk: 64%					
		High risk: 64%					
		····g·····e····e···					
		Groups comparable at					
		baseline? Yes					
			Hydration versus no hy	dration at contrast administrat	ion		
Chen,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Author's conclusion:
2008	RCT	Patients with myocardial	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
		ischemia (angina or			6 months	(include 95%CI and p-	Patients with CIN and
	Setting: in-	positive exercise	sCr<1.5mg/dL:	sCr<1.5mg/dL:		value if available):	preexisting renal
	and	treadmill) scheduled for	0.45% saline given	No hydration	Loss-to-follow-up:		insufficiency had
	outpatients,	percutaneous coronary	intravenously at a rate of 1		Not reported	CIN	worse clinical
	multicentre	intervention (PCI) in one	ml/kg/h starting from 12 h			(=increase in SCrN0.5	outcomes. Hydration
	study	of the three	before	sCr ≥1.5mg/dL:	Incomplete	mg/dl at 48 h after	with 0.45% sodium
		participating centers	scheduled time for coronary	twice orally loading dose of	outcome data:	PCI)	chloride alone had no
	Country:	Fuchasian axit 1	angiogram	1200 mg NAC at 12 h before	Not reported		potential effect on
	China	Exclusion criteria:		scheduled time for coronary		sCr<1.5mg/dL:	the occurrence of
	Source of	(1) the coronary		angiogram and immediately		l: 6.7% C: 7.0%	CIN in patients with normal renal
	Source of	anatomy not suitable for	sCr >1 Emg/dL	after procedure			function.
	funding: not	PCI;	sCr ≥1.5mg/dL:			p>0.05	Combination of
	reported	(2) emergency coronary artery bypassgrafting	1) 0.45% saline given intravenously at a rate of 1				hydration with ATLS
			ml/kg/h starting from 12 h			cCr >1 5mg/dl ·	could reduce the
		(CABG) being required;	minkg/mstarting from 12 h			sCr ≥1.5mg/dL:	could reduce the

		(2) patients in chronic	before scheduled time for			1: 21.3%	incidence of CIN in
		(3) patients in chronic				C: 34.0%	
		peritoneal or	coronary angiogram				patients at high risk.
		hemodialytic treatment;	2) twice orally loading dose			P<0.001	
		(4) acute myocardial	of 1200 mg NAC at 12 h				
		infarction (AMI) at	before scheduled time for				Groups comparable
		admission;	coronary angiogram and				at baseline? Unclear
		(5) no written formal	immediately after				(patient data not
		consent from patients	procedure				reported for
							intervention and
		N total at baseline:					control group
		sCr<1.5mg/dL					separately)
		Intervention: 330					
		Control: 330					
		sCr ≥1.5mg/dL					
		Intervention: 188					
		Control: 188					
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		not reported					
		not reported					
		Sex: %M					
		sCr<1.5mg/dL					
		85%					
		sCr ≥1.5mg/dL					
		82%					
		Groups comparable at					
		baseline? Unclear					
		(patient data not					
		reported for					
		intervention and control					
		group separately)					
Jurado-	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
Roman,	RCT	patients who were	(treatment/procedure/test):	(treatment/procedure/test):	up:	and effect size	
,	1		((<u> </u>		

2014		admitted			3 days	(include 95%CI and p-	In conclusion,
	Setting: in-	for STEMI and	Hydration:	No hydration		value if available):	intravenous saline
	and	underwent a PPCI from	isotonic saline at an infusion	Prior to PPCI	Loss-to-follow-up:		hydration during
	outpatients,	July 2012 to	rate of 1 ml/kg/h since the		Not reported	CIN	PPCIreduced the risk
	single centre	November 2013 at our	beginning of the procedure			(=a ≥25% or ≥0.5	of CIN to 48%.
	study	institution.	and during the following 24		Incomplete	mg/dl increase in	Given the higher
	-		hours.		outcome data:	serum a _25% or _0.5	incidence of CIN in
	Country: Spain	Exclusion criteria:			Not reported	mg/dl increase in	emergentprocedures,
		1) end-stage renal	Prior to PPCI			serum)	and its morbidity
	Source of	failure requiring dialysis,			Crossover		and mortality,
	funding: not	2) cardiac arrest,			between study	CIN was observed in	preventive hydration
	reported	3) severe heart failure			arms: 28%	14% of patients:	should be mandatory
		(Killip III to IV)			How this was	I: 11%	in them unless
					handled in the	C: 21%	contraindicated.
		N total at baseline:			data analysis is	(p=0.016).	
		Intervention: 204			not reported.		
		Control: 204			74 patients	In multivariate	Crossover between
					changed from no	analysis, the only	study arms: 28%
		Important prognostic			hydration to	predictors of CIN	How this was
		<u>factors</u> ² :			hydration group	were:	handled in the data
		For example			because of sever	1) hydration (OR=0.29	analysis is not
		age ± SD:			hypotension	[0.14 to 0.66];	reported.
		l:62 ± 14			42 patients were	p=0.003)	
		C: 64 ± 12			changed from	2) hemoglobin before	
					hydration to no	the procedure	
		Sex:			hydration group	(OR=0.69 [0.59 to	
		I: 72% M			because they	0.88]; p <0.0001)	
		C: 75% M			developed heart		
					failure		
		Groups comparable at					
		baseline? Yes					
Kooiman,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of follow-	Outcome measures	Authors' conclusion:
2014	RCT	1) Inpatients and	(treatment/procedure/test):	(treatment/procedure/test):	<u>up</u> :	and effect size	
		outpatients with high			96 hours for	(include 95%CI and p-	Our results suggest
	Setting:in- and	clinical suspicion of	Sodium bicarbonate	No hydration prior to CTPA	laboratory	value if available):	that preventive
	outpatients,	acute PE requiring CTPA	hydration prior to CTPA		parameters		hydration could be
	single centre	(i.e. Wells score \geq 4 or			2 months for	CI-AKI	safely withheld in

	D dim on loss 1	250 mil internet 1.401	alternation t	(and the in the interview of the interv	
	D-dimer levels	250 mL intravenous 1.4%	clinical outcomes	(=creatinine increase	CKD patients
Country: the	> 500 ng mL ⁻¹).	sodium bicarbonate 1 h		$> 25\% /> 0.5 \text{ mg dL}^{-1}$	undergoing CTPA for
Netherlands	2) at least 18 years old	before CTPA without	Loss-to-follow-up:	I: 5/71 (7%)	suspected acute
	3) CKD (estimated	hydration after CTPA.	Intervention:	C: 6/67 (9%)	pulmonary
Source of	glomerular filtration		2/71 (3%)	RR: 1.29, 95%	embolism. This will
funding: non-	rate		1 withdrew	confidence interval	facilitate
commercial	[eGFR] < 60 mL min		informed consent	0.41-4.03	management of
	$^{-1}/1.73$ m ² estimated by		1 died 24 hours		these patients and
	using the Modification		after CTPA	None of the CI-AKI	prevents delay in
	of Diet in Renal Disease			patients developed a	diagnosis as well as
	formula		Control:	need for dialysis.	unnecessary start of
			2/67 (3%)		anticoagulant
	Exclusion criteria:		Lost to follow-up		treatment while
	1) pregnancy,				receiving volume
	2) previous contrast		Incomplete		expansion.
	administration within		outcome data:		
	the past 7 days,		As above		
	3) documented allergy				
	for iodinated contrast				
	media,				
	4) hemodynamic				
	instability (systolic blood				
	pressure < 100 mm Hg)				
	5) participation in				
	another trial				
	N total at baseline:				
	Intervention: 71				
	Control: 67				
	Important prognostic				
	factors ² :				
	For example				
	age ± SD:				
	l: 71 ± 13				
	$C: 70 \pm 12$				
	C. 70 ± 12				
		1	1	1	

Maioli, 2011	Type of study: RCT Setting: in- and outpatients, single centre Country: Italy Source of funding: not reported	Sex: I: 48% M C: 52% M Groups comparable at baseline? Yes Inclusion criteria: 1) patients with STEMI who were candidates for primary PCI Exclusion criteria: 1) contrast medium administration within the previous 10 days, 2) end-stage renal failure requiring dialysis, 3) refusal to give informed consent N total at baseline: Intervention: 154 Control: 153 Important prognostic factors ² : For example age ± SD: I:65 ± 13 C: 64 ± 12 Sex: I: 77% M C: 73% M	Describe intervention (treatment/procedure/test): Patients assigned to early hydration were administered a bolus of 3 mL/kg of sodium bicarbonate solution (154 mEq/L in dextrose and water) in 1 hour, starting in the emergency room, followed by infusion of 1 mL/kg per hour for 12 hours after PCI. Hydration rate was reduced to 0.5 mL/kg per hour in patients with left ventricular ejection fraction (EF) <40% or New York Heart Association class III–IV in both groups.	Describe control (treatment/procedure/test): No hydration prior to PCI.	Length of follow- UP: 3 days Loss-to-follow-up: Intervention: 4/150 (3%) 1 had emergency procedure 3 no PCI Control: 3/153 (2%) 1 had emergency procedure 2 no PCI Incomplete outcome data: As above	Outcome measures and effect size (include 95%CI and p- value if available): CI-AKI (=an increase in serum creatinine of \geq 25% or 0.5 mg/dL over the baseline value within 3 days after administration of the contrast medium) I: 12% C: 27% P<0.001 Death I: 3 (2%) C: 8 (5%) p>0.05 Hemofiltration I: 2 (1%) C: 1 (1%) p>0.05	Authors' conclusion: Adequate intravenous volume expansion may prevent CI-AKI in patients undergoing primary PCI. A regimen of preprocedure and postprocedure hydration therapy with sodium bicarbonate appears to be more efficacious than postprocedure hydration only with isotonic saline.
						· · ·	

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

AKI: acute kidney injury; CI-AKI: contrast induced acute kidney injury; CIN: contrast induced nephropathy; CT: Computed Tomography; CTPA: Computed Tomography of the pulmonary artery; eGFR: estimated glomerular filtration ration; ia: intra-arterial; IOCM: iso-osmolar contrast medium; iv: intravenous; LOCM: low osmolair contrast medium; OR: odds ratio; PCI: Percutaneous Coronary Intervention; PE: pulmonary embolism; PPCI: primary Percutaneous Coronary Intervention; RCT: randomized controlled trial; RR: relative risk; sCr: serum creatinine; STEMI: ST-elevation myocardial infarction

Risk of bias assessment diagnostic accuracy studies (QUADAS II, 2011)

Research question:

Study reference	Patient selection	Index test	Reference standard	Flow and timing	Comments with respect to applicability
Duan, 2017	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
2 000.1 2027	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes, consecutive	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear		oncical	No
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		

	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Lian, 2017	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				<u>analysis?</u>	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Abellas-	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
Sequeiros,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
2016	Yes, consecutive	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	<u>index test?</u>		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by

	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias?	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	Were all patients included in the analysis? Yes CONCLUSION Could the patient flow have introduced bias?	<u>the reference standard does not</u> <u>match the review question?</u> No
Araujo, 2016	Was a consecutive or random sample of patients enrolled? Yes, consecutive Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Unclear If a threshold was used, was it pre-specified? Yes	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test? Unclear	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias? RISK: LOW	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	CONCLUSION Could the patient flow have introduced bias? RISK: LOW	
Chou, 2016	Was a consecutive or random sample of patients enrolled? Unclear Was a case-control design avoided?	Were the index test results interpreted without knowledge of the results of the reference standard? Unclear	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	Are there concerns that the included patients do not match the review question? No Are there concerns that the

	No.	If a thread all supervised super th	near the internated with east	unformer en etc. u de ud2	indoutest its soudust on
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Lazaros, 2016	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
L				I	J I

	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Liu, 2016	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Unclear			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Yes	index test?		review question?
	inappropriate exclusions?		Unclear	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Aykan, 2013	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
•	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
		I Contraction of the second seco	1		
					target condition as defined by

				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Bartholomew,	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
2004	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		<u>standard?</u>	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Chen, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or

1		10 10			
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	<u>index test?</u>		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
		have introduced bids.	have indicated blast		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Fu, 2012	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
-, -	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review guestion?
	105	standard?	Yes	Unclear	No
	Was a case-control design	Yes	105	oncical	110
	avoided?	105	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	163	pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?	Tes	
		Unclear		Did notionto no ocivo the come	review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	

Gao, 2013	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
000, 2015	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
	103	standard?	Yes	Unclear	No
	Was a case-control design	Yes	165	Officieal	NO
	avoided?	Tes	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	res			Yes	interpretation differ from the
	Did the study evoid	<u>pre-specified?</u> Unclear	knowledge of the results of the	res	
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Gurm, 2013	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
		of the results of the reference	condition?	and reference standard?	included patients do not match the review question?
	sample of patients enrolled?				included patients do not match
	sample of patients enrolled? Yes Was a case-control design	of the results of the reference	<u>condition?</u> Yes	and reference standard? Unclear	included patients do not match the review question? No
	sample of patients enrolled? Yes	of the results of the reference standard?	<u>condition?</u> Yes <u>Were the reference standard</u>	and reference standard?	included patients do not match the review question? No <u>Are there concerns that the</u>
	sample of patients enrolled? Yes Was a case-control design	of the results of the reference standard? Yes If a threshold was used, was it	<u>condition?</u> Yes	and reference standard? Unclear	included patients do not match the review question? No
	sample of patients enrolled? Yes Was a case-control design avoided?	of the results of the reference standard? Yes	<u>condition?</u> Yes <u>Were the reference standard</u>	and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No <u>Are there concerns that the</u>
	sample of patients enrolled? Yes Was a case-control design avoided?	of the results of the reference standard? Yes If a threshold was used, was it	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u>	and reference standard? Unclear Did all patients receive a reference standard?	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or
	sample of patients enrolled? Yes Was a case-control design avoided? Yes	of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u>	and reference standard? Unclear Did all patients receive a reference standard?	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the
	sample of patients enrolled? Yes <u>Was a case-control design</u> <u>avoided?</u> Yes <u>Did the study avoid</u>	of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u> <u>index test?</u>	and reference standard? Unclear <u>Did all patients receive a</u> <u>reference standard?</u> Yes	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question?
	sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u> <u>index test?</u>	and reference standard? Unclear <u>Did all patients receive a</u> <u>reference standard?</u> Yes <u>Did patients receive the same</u>	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question?
	sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u> <u>index test?</u>	and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the
	sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	<u>condition?</u> Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u> <u>index test?</u>	and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No

1				Yes	No
	CONCLUSION	CONCLUCION	CONCLUCION		NO
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Inohara, 2015	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review guestion?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review guestion?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Ivanes, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the

1	Did the study avoid	Unclear	index test?		review guestion?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Ji, 2015	Was a consecutive or random	Were the index test results	Is the reference standard likely		Are there concerns that the
JI, 2015	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	Was there an appropriate interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
	165	standard?	Yes	Unclear	No
	Was a case-control design	Yes	Tes	Officieal	NO
	avoided?	103	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Kul, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the

1	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	have introduced bias?	RISK: LOW	RISK: LOW	
Maioli, 2010	RISK: LOW Was a consecutive or random	RISK: LOW	RISK: LOW		Are there concerns that the
Maioli, 2010				RISK: LOW Was there an appropriate interval between index test(s)	Are there concerns that the included patients do not match
Maioli, 2010	Was a consecutive or random	RISK: LOW Were the index test results	RISK: LOW Is the reference standard likely	Was there an appropriate	
Maioli, 2010	Was a consecutive or random sample of patients enrolled?	RISK: LOW Were the index test results interpreted without knowledge	RISK: LOW <u>Is the reference standard likely</u> <u>to correctly classify the target</u>	Was there an appropriate interval between index test(s)	included patients do not match
Maioli, 2010	Was a consecutive or random sample of patients enrolled?	RISK: LOW <u>Were the index test results</u> <u>interpreted without knowledge</u> <u>of the results of the reference</u>	RISK: LOW <u>Is the reference standard likely</u> <u>to correctly classify the target</u> <u>condition?</u>	Was there an appropriate interval between index test(s) and reference standard?	included patients do not match the review question?
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes	RISK: LOW <u>Were the index test results</u> <u>interpreted without knowledge</u> <u>of the results of the reference</u> <u>standard?</u>	RISK: LOW <u>Is the reference standard likely</u> <u>to correctly classify the target</u> <u>condition?</u>	Was there an appropriate interval between index test(s) and reference standard?	included patients do not match the review question?
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without	Was there an appropriate interval between index test(s) and reference standard? Unclear	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the review question?
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not
Maioli, 2010	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	RISK: LOW Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	RISK: LOW Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by

	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION] [
		Could the conduct or	Could the reference standard.		
	Could the selection of patients			Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Mehran, 2004	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review guestion?
	inappropriate exclusions?	Oncical	Yes	Did patients receive the same	No
	Yes		105	reference standard?	110
	103			Yes	Are there concerns that the
				103	target condition as defined by
				Were all patients included in the	the reference standard does not
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	NO
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Mizuno, 2015	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
		Uncical			

	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard? Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				<u>analysis?</u> Yes	match the review question? No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Raposeiras-	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
Roubín, 2013	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design avoided?	Yes	Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	<u>Are there concerns that the</u> index test, its conduct, or
	163	pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?	103	review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes			reference standard?	-
				Yes	Are there concerns that the
					target condition as defined by
				Were all patients included in the	the reference standard does not
				<u>analysis?</u>	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test have introduced bias?	its conduct, or its interpretation have introduced bias?	introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Sgura, 2010	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
2000, 2010	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match

	Yes	of the results of the reference	condition?	and reference standard?	the review question?
		standard?	Yes	Unclear	No
	Was a case-control design	Yes			
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Did the study avoid	Unclear	index test?		review question?
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Yes		105	reference standard?	
	105			Yes	Are there concerns that the
				Tes	target condition as defined by
				Mara all patients included in the	the reference standard does not
				Were all patients included in the	
				analysis?	match the review question?
				Yes	No
	CONCLUSION:	CONCLUSION:	CONCLUSION:	CONCLUSION	
	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
		have introduced bias?	have introduced bias?		
1					
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
Tziakas, 2013	RISK: LOW Was a consecutive or random	RISK: LOW Were the index test results	RISK: LOW <u>Is the reference standard likely</u>	RISK: LOW Was there an appropriate	Are there concerns that the
Tziakas, 2013					Are there concerns that the included patients do not match
Tziakas, 2013	Was a consecutive or random	Were the index test results interpreted without knowledge	Is the reference standard likely	Was there an appropriate interval between index test(s)	included patients do not match
Tziakas, 2013	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge of the results of the reference	Is the reference standard likely to correctly classify the target	Was there an appropriate	
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes	Were the index test results interpreted without knowledge	Is the reference standard likely to correctly classify the target condition?	Was there an appropriate interval between index test(s) and reference standard?	included patients do not match the review question?
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference standard?	Is the reference standard likely to correctly classify the target condition? Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear	included patients do not match the review question? No
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes <u>Was a case-control design</u> avoided?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes	Is the reference standard likely to correctly classify the target condition? Yes Were the reference standard	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No Are there concerns that the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard?	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the review question?
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard?	included patients do not match the review question? No <u>Are there concerns that the</u> index test, its conduct, or interpretation differ from the review question? No
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis?	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question?
Tziakas, 2013	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions?	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified?	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> results interpreted without knowledge of the results of the index test?	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the	included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not

Victor, 2014	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge	<u>Is the reference standard likely</u> to correctly classify the target	Was there an appropriate interval between index test(s)	Are there concerns that the included patients do not match
N# 1 0011	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
		have introduced bias?	have introduced bias?		
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
	CONCLUSION: Could the selection of patients	CONCLUSION: Could the conduct or	CONCLUSION: Could the reference standard,	Could the patient flow have	
	CONCLUSION:	CONCLUSION:	CONCLUSION:	Yes CONCLUSION	No
				analysis?	match the review question?
				Were all patients included in the	the reference standard does not
					target condition as defined by
				Yes	Are there concerns that the
	Yes			reference standard?	
	inappropriate exclusions?		Yes	Did patients receive the same	No
	Did the study avoid	Unclear	index test?		review question?
		pre-specified?	knowledge of the results of the	Yes	interpretation differ from the
	Yes	If a threshold was used, was it	results interpreted without	reference standard?	index test, its conduct, or
	avoided?		Were the reference standard	Did all patients receive a	Are there concerns that the
	Was a case-control design	Yes			
		standard?	Yes	Unclear	No
	Yes	of the results of the reference	condition?	and reference standard?	the review question?
,	sample of patients enrolled?	interpreted without knowledge	to correctly classify the target	interval between index test(s)	included patients do not match
Tziakas, 2014	Was a consecutive or random	Were the index test results	Is the reference standard likely	Was there an appropriate	Are there concerns that the
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	
		have introduced bias?	have introduced bias?		
	have introduced bias?	interpretation of the index test	its conduct, or its interpretation	introduced bias?	
1	Could the selection of patients	Could the conduct or	Could the reference standard,	Could the patient flow have	

	Yes CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test	CONCLUSION: Could the reference standard, its conduct, or its interpretation	reference standard? Yes <u>Were all patients included in the</u> <u>analysis?</u> Yes CONCLUSION Could the patient flow have introduced bias?	Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	RISK: LOW	have introduced bias? RISK: LOW	have introduced bias? RISK: LOW	RISK: LOW	
Lin, 2014	Was a consecutive or random sample of patients enrolled? Yes Was a case-control design avoided? Yes Did the study avoid inappropriate exclusions? Yes	Were the index test results interpreted without knowledge of the results of the reference standard? Yes If a threshold was used, was it pre-specified? Unclear	Is the reference standard likely to correctly classify the target condition? Yes <u>Were the reference standard</u> <u>results interpreted without</u> <u>knowledge of the results of the</u> <u>index test?</u> Yes	Was there an appropriate interval between index test(s) and reference standard? Unclear Did all patients receive a reference standard? Yes Did patients receive the same reference standard? Yes Were all patients included in the analysis? Yes	Are there concerns that the included patients do not match the review question? No Are there concerns that the index test, its conduct, or interpretation differ from the review question? No Are there concerns that the target condition as defined by the reference standard does not match the review question? No
	CONCLUSION: Could the selection of patients have introduced bias?	CONCLUSION: Could the conduct or interpretation of the index test have introduced bias?	CONCLUSION: Could the reference standard, its conduct, or its interpretation have introduced bias?	CONCLUSION Could the patient flow have introduced bias?	
	RISK: LOW	RISK: LOW	RISK: LOW	RISK: LOW	

Judgments on risk of bias are dependent on the research question: some items are more likely to introduce bias than others, and may be given more weight in the final conclusion on the overall risk of bias per domain:

Patient selection:

- Consecutive or random sample has a low risk to introduce bias.
- A case control design is very likely to overestimate accuracy and thus introduce bias.
- Inappropriate exclusion is likely to introduce bias.

Index test:

- This item is similar to "blinding" in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.
- Selecting the test threshold to optimise sensitivity and/or specificity may lead to overoptimistic estimates of test performance and introduce bias.

Reference standard:

- When the reference standard is not 100% sensitive and 100% specific, disagreements between the index test and reference standard may be incorrect, which increases the risk of bias.
- This item is similar to "blinding" in intervention studies. The potential for bias is related to the subjectivity of index test interpretation and the order of testing.

Flow and timing:

- If there is a delay or if treatment is started between index test and reference standard, misclassification may occur due to recovery or deterioration of the condition, which increases the risk of bias.
- If the results of the index test influence the decision on whether to perform the reference standard or which reference standard is used, estimated diagnostic accuracy may be biased.
- All patients who were recruited into the study should be included in the analysis, if not, the risk of bias is increased.

Judgement on applicability:

Patient selection: there may be concerns regarding applicability if patients included in the study differ from those targeted by the review question, in terms of severity of the target condition, demographic features, presence of differential diagnosis or co-morbidity, setting of the study and previous testing protocols.

Index test: if index tests methods differ from those specified in the review question there may be concerns regarding applicability.

Reference standard: the reference standard may be free of bias but the target condition that it defines may differ from the target condition specified in the review question.

Evidence table for diagnostic test accuracy studies

Research question:

Study	Study	Patient	Index test	Reference test	Follow-up	Outcome measures and	Comments
reference	characteristics	characteristics	(test of interest)			effect size	
Aykan, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference	Time between the index	Outcome measures and	Internal validation only
	study ¹ : cohort	Acute STEMI	SYNTAX score	test ³ :	test en reference test: 72	effect size (include 95%Cl	
	study	patients within		≥25% increase of serum	hours	and p-value if available) ⁴ :	Patients with previous
		12 hours of		creatinine			coronary artery bypass
	Setting: in-	symptom onset		concentrations form	For how many	Mehran:	were excluded
	and		Comparator test ² :	baseline within 72 hours	participants were no	Sens: 73%	

 ¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)
 ² Comparator test is vergelijkbaar met de C uit de PICO van een interventievraag. Er kunnen ook meerdere tests worden vergeleken. Voeg die toe als comparator test 2 etc. Let op: de comparator test kan nooit de referentiestandaard zijn.

	outpatients	Exclusion	Mehran score	after PCI	complete outcome data	Spec: 89%	
		criteria:			available?		
	Country:	Patients with			NR	SYNTAX:	
	, Turkey	previous				Sens: 79%	
	,	coronary artery			Reasons for incomplete	Spec: 89%	
	Conflicts of	bypass			outcome data described?		
	interest: not				NR	Mehran:	
	reported	N= 402				Cut-off value: 12.5	
	-					AUC: 0.68 (95% CI: 0.63 –	
		Prevalence: 32%				0.74, p<0.001)	
		Mean age ± SD:				SYNTAX:	
		63 ± 13				Cut-off value: 31.5	
						AUC: 0.66 (95% CI: 0.60 –	
		Sex: 76 % M				0.71, p<0.001)	
Bartholomew,	Type of study:	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
2004	cohort	Coronary	RCIN risk score	≥1.0mg/dL increase in	test en reference test: 48	effect size (include 95%Cl	
		interventional		serum creatinine from	hours	and p-value if available):	
	Setting: in-	procedures		baseline within 48 hours			
	and	(single center)		of PCI	For how many	External validation	
	outpatients				participants were no	Cohort 1: patients	
		Exclusion			complete outcome data	admitted for elective PCI	
	Country:	criteria: -			available?	N=2689	
	United States				NR	Discrimination: 0.59	
	of America	N= 10 481				Calibration: NR	
					Reasons for incomplete		
	Conflicts of	Incidence of			outcome data described?	Cohort 2: patients	
	interest:	events:			NR	admitted for elective or	
	commercial	Derivation				emergency PCI	
		cohort: 2.8%				N=488	
		Validation				Discrimination: 0.58	
		cohort: 1.2%				Calibration: NR	

³ De referentiestandaard is de test waarmee definitief wordt aangetoond of iemand al dan niet ziek is. Idealiter is de referentiestandaard de Gouden standaard (100% sensitief en 100% specifiek). Let op! dit is niet de "comparison test/index 2".

⁴ Beschrijf de statistische parameters voor de vergelijking van de indextest(en) met de referentietest, en voor de vergelijking tussen de indextesten onderling (als er twee of meer indextesten worden vergeleken).

Chen, 2014	Type of study ⁴ : cohort study Setting: in- and outpatients Country: China Conflicts of interest: not reported	Mean age ± SD: 65 ± 12 Sex: 67% M Inclusion criteria: patients receiving PCI, single center Exclusion criteria: - N=1500 ncidence of events: Derivation cohort: 16% Validation cohort: 17% Mean age ± SD: 64 ± 10	Describe index test: "preprocedural risk scoring system"	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creat8inine within 5 days of PCI	Time between the index test en reference test: 5 days For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): Discrimination/calibration: 0.82 P=0.89 Risk score range associated with PC-AKI risk: Low: 5.3% Moderate: 19.9% High: 32.5% Very high: 59.5%	Internal validation only
		64 ± 10 Sex:68 % M					
Fu, 2012	Type of study ⁵ : cohort study Setting: in- and	Inclusion criteria: patients undergoing PCI, single center Exclusion	Describe index test: "risk score for contrast induced nephropathy in elderly patients"	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 48-72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no	Outcome measures and effect size (include 95%Cl and p-value if available): External validation Elderly patients at same	

⁴ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ⁵ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	outpatients Country: China Conflicts of interest: not reported	criteria: - N= 668 Prevalence: 16% Mean age ± SD: 70 ± 6 Sex: 48% M			complete outcome data available? NR Reasons for incomplete outcome data described? NR	institution N=277 Discrimination: 0.79 Calibration: p>0.05	
Gao, 2004	Type of study ⁶ : cohort study Setting: in- and outpatients Country: China Conflicts of interest: not reported	Inclusion criteria: Coronary angiography or PCI, single center Exclusion criteria: - N=2764 Incidence of events: Derivation cohort: 5.5% Validation cohort: 5.0% Mean age ± SD: 60 ± 11 Sex: 71% M	Describe index test: "simple risk score for prediction of CIN" Comparator test: Mehran risk score	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): Discrimination / calibration: 0.76 p>0.05 AUC: 1) "simple risk score": 0.75 (95% Cl: 0.71 – 0.78) 2) Mehran: 0.57 (95%Cl:0.54 – 0.60) Incidence of events: Derivation cohort: 4.6% Validation cohort: 4.2%	Internal validation only
Ghani, 2009	Type of study ⁷ : cohort study	Inclusion criteria: patients undergoing PCI,	Describe index test: "simple risk score for CIN"	Describe reference test: >0.5 mg/dL increase in serum creatinine within	Time between the index test en reference test: 48 hours	Outcome measures and effect size (include 95%CI and p-value if available):	Internal validation only

⁶ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		single center		48 hours of PCI			
	Setting: in- and outpatients Country: Kuwait Conflicts of interest: not reported	single center Exclusion criteria:- N= 247 Incidence of events: Derivation cohort: 5.5% Validation cohort: 5.0% Mean age ± SD: 63 ± 10		48 hours of PCI	For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Risk score range associated with PC-AKI: <4: 9.2% 5-8: 32% 9-12: 54% >12: 84%	
Gurm, 2014	Type of study ⁸ : cohort study Setting: in- and outpatients Country: United States of America / the Netherlands	Sex: 68% M Inclusion criteria: patients undergoing PCI, multiple center Exclusion criteria: 1) patients on dialysis 2) patients with missing serum creatinine values N= 48001	Describe index test: "novel easy-to-use computational tool"	Describe reference test: >0.5 mg/dL increase in serum creatinine within 7 days of PCI	Time between the index test en reference test: 7 days For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): AUC: 0.88 Risk score range associated with PC-AKI: Low: 0.5% Medium: 2.8% High: 13% Incidence of events: Derivation cohort: 2.6%	Internal validation only

⁷ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ⁸ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

(Lijmer et al., 1999)

	Conflicts of interest: not reported	Prevalence: 3%				Validation cohort: 2.5%	
		Mean age ± SD: 65 ± 12					
Inohara, 2014	Type of study ⁹ : cohort study Setting: in- and outpatients Country: Japan Conflicts of interest: not reported	Sex: NR Inclusion criteria: Exclusion criteria: N= 3957 Prevalence: 9% Mean age ± SD: 69 ± 11 Sex: 79% M	Describe index test: "pre-percutaneous cornary intervention risk model"	Describe reference test: An increase in serum creatinine of 50% or 0.3mg/dL compared with baseline	Time between the index test en reference test: 30 days For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): External validation: N=1979 Discrimination: c-statistic 0.79	
Ivanes, 2014	Type of study ¹⁰ : cohort study Setting: in- and outpatients Country: France	Inclusion criteria: PCI, single center Exclusion criteria: - N=322 Prevalence:9% Mean age ± SD:	Describe index test: Mehran risk score	Describe reference test: ≥25% or 44.2µmol/L increase in serum creatinine following contrast administration	Time between the index test en reference test: 48 hours For how many participants were no complete outcome data available? NR	Outcome measures and effect size (include 95%Cl and p-value if available): AUC: 0.59 CIN incidence: 9%	Internal validation only

⁹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ¹⁰ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	Conflicts of interest: not	64 ± 14			Reasons for incomplete outcome data described?		
	reported	Sex: 66% M			NR		
Jin, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹¹ :	Acute	Mehran risk score	>0.5 mg/dL	test en reference test: 48	effect size (include 95%CI	
	cohort study	myocardial		(44.2µmol/L) or 25%	hours	and p-value if available):	
		infarction		increase in serum			
	Setting: in-	patients		creatinine within 48	For how many	Risk score range	
	and	undergoing PCI		hours of PCI	participants were no	associated with PC-AKI:	
	outpatients				complete outcome data	Low: 12%	
		Exclusion			available?	Medium: 35%	
	Country:	criteria: -			NR	High: 36%	
	China						
		N= 1041			Reasons for incomplete		
	Conflicts of				outcome data described?		
	interest: not	Prevalence: 14%			NR		
	reported						
		Mean age ± SD:					
		68 ± 12					
		Sex: 52% M					
Kul, 2015	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹² :	patients with	Zwolle risk score	>0.5 mg/dL or 25%	test en reference test: 72	effect size (include 95%Cl	
	cohort study	acute STEMI and		increase in serum	hours	and p-value if available):	
		undergoing		creatinine within 72			
	Setting: in-	emergency PCI		hours of PCI	For how many	1) Zwolle score >2	
	and		Comparator test:		participants were no	Sens: 76%	
	outpatients	Exclusion	Mehran risk score		complete outcome data	Spec: 75%	
		criteria: -			available?	AUC: 0.85	
	Country:				NR		
	Turkey	N= 314				2) Mehran score > 5	
					Reasons for incomplete	Sens: 71%	

¹¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ¹² In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	Conflicts of interest: not reported	Prevalence: 12% Mean age ± SD: 56 ± 11 Sex: 81% M			outcome data described? NR	Spec: 74% AUC:0.79	
Lin, 2015	Type of study ¹³ : cohort study Setting: in- and outpatients Country: Taiwan / Egypt Conflicts of interest: not reported	Inclusion criteria: PCI, single center (including emergency PCI) Exclusion criteria: - N= 516 Prevalence: 12% Mean age ± SD: 64 ± 11 Sex: 83% M	Describe index test: 1) "comprehensive risk score model", WHC model 2) Bartholomew model 3) Mehran model 4) Tziakas model 5) Ghain model	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 72 hours of PCI	Time between the index test en reference test: 72 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): AUC: 1) own model: 0.92 (95%Cl: 0.88 – 0.96) 2) Bartholomew model 0.91 (95%Cl: 0.87 – 0.95) 3) Mehran model: 0.90 (95%Cl: 0.86 – 0.94) 4) Tziakas model: 0.70 (95%Cl: 0.58 – 0.83) 5) Ghain model: 0.65 (95% Cl: 0.53 – 0.78) External validation: n=241 Discrimination and calibration NR	
Maioli, 2010	Type of study ¹⁴ : cohort study Setting: in-	Inclusion criteria: patients with an indication for coronary angiography or	Describe index test: Global Registry for Acute Coronary Events (GRACE) risk score	Describe reference test: >0.5 mg/dL (44.2µmol/L) or 25% increase in serum creatinine within 5 days	Time between the index test en reference test: 5 days For how many	Outcome measures and effect size (include 95%Cl and p-value if available): GRACE	Risk score range associated with PC-AKI risk: 0-1: 0% 2-3: 1%
	and outpatients	PCI, single center	Comparator test:	of PCI	participants were no complete outcome data	Cut-off 160 Sens: 79%	4: 2% 5: 6%

¹³ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ¹⁴ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

		Exclusion	Mehran risk score		available?	Spec: 61%	6: 12%
	Country: Italy	criteria: -			NR		7: 19%
						Mehran	8: 24%
	Conflicts of	N=1281			Reasons for incomplete	NR	9: 36%
	interest: not	-			outcome data described?		10: 50%
	reported	Prevalence: 3%			NR	Incidence of events:	
						Derivation cohort: 3.0%	
		Mean age ± SD:				Validation cohort: NR	
		69 ± 10					
						AUC:	
		Sex: 67% M				1) GRACE: 0.72 (0.3) and	
						0.69 (0.5)	
						2) Mehran: 0.78 (0.3) and	
						0.84 (0.5)	
						External validation	
						N=502	
						Discrimination and	
						calibration NR	
Marenzi,	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
2004	study ¹⁵ :	patients referred	Marenzi risk score	>0.5 mg/dL increase in	test en reference test: 5	effect size (include 95%Cl	
	cohort study	for PCI for		serum creatinine within	days	and p-value if available):	
		STEMI, single		5 days of PCI			
	Setting: in-	center			For how many	External validation	
	and				participants were no	N=891	
	outpatients	Exclusion			complete outcome data	Discrimination 0.57 and	
		criteria:			available?	calibration NR	
	Country: Italy				NR		
		N= 218					
	Conflicts of				Reasons for incomplete		
	interest: not	Incidence of			outcome data described?		
	reported	events:			NR		
		Derivation					
		cohort: 19%					

¹⁵ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		Validation cohort: 14% M					
Mehran, 2004	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
	study ¹⁶ :	patients referred	Mehran risk score	>0.5 mg/dL or 25%	test en reference test: 48	effect size (include 95%Cl	
	cohort study	for PCI, single		increase in serum	hours	and p-value if available):	
		center		creatinine within 48			
	Setting: in-			hours of PCI	For how many	For Creatinine:	
	and	Exclusion			participants were no	Discrimination: 0.69	
	outpatients	criteria: -			complete outcome data	Validation: p=0.43	
					available?		
	Country:	N= 5571			NR	For eGFR:	
	United States					Discrimination: 0.70	
	of America	Prevalence: 14%			Reasons for incomplete	Validation: p=0.42	
					outcome data described?		
	Conflicts of	Mean age ± SD:			NR	External validation	
	interest: not	64 ± 11				Cohort 1: patients	
	reported					undergoing cardiac	
		Sex: 71% M				catheterization or PCI,	
						single center	
						N=3945	
						Discrimination: 0.57	
						Calibration: NR	
						Cohort 2: patients	
						admitted for elective or	
						emergency PCI, single	
						center	
						N=5571	
						Discrimination: 0.59	
						Calibration: NR	
Mizuno, 2014	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹⁷ :	patients	Mehran Risk score	>0.5 mg/dL or 25%	test en reference test: 3	effect size (include 95%Cl	
	cohort study	undergoing a PCI		increase in serum	days	and p-value if available):	

¹⁶ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999)

		for STEMI, single	(and red cell	creatinine within 3 days			
	Setting: in-	center	distribution width)	of PCI	For how many	AUC Mehran: 0.72 (0.54 –	
	and				participants were no	0.90)	
	outpatients	Exclusion			complete outcome data		
		criteria: -			available?		
	Country:				NR		
	Japan	N= 102					
					Reasons for incomplete		
	Conflicts of	Prevalence: 10%			outcome data described?		
	interest: not				NR		
	reported	Mean age ± SD:					
		62 ± 14					
		Sex: 78 % M					
Raposeiras-	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
Roubín, 2013	study ¹⁸ :	Patients with	GRACE risk score	≥25% or ≥0.3mg/dL (or	test en reference test: 72	effect size (include 95%Cl	
	cohort study	myocardial		0.5) rise in serum	hours	and p-value if available):	
	c	infarction after		creatinine levels after			
	Setting: in-	corronary		72 hours	For how many	GRACE risk score >140	
	and	angiography			participants were no	was an independent predictor of CIN	
	outpatients	Evolution			complete outcome data	predictor of CIN	
	Country Croin	Exclusion criteria:			available? NR		
	Country: Spain	cillena.			INK		
	Conflicts of	-			Reasons for incomplete		
	interest: not	N=202			outcome data described?		
	reported	11-202			NR		
	reported	Prevalence: 28%					
		Mean age ± SD:					
		63 ± 13					
		-					

¹⁷ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ¹⁸ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

(Lijmer et al., 1999)

		Sex: 75% M					
Sgura, 2010	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	Internal validation only
	study ¹⁹ :	patients	Mehran risk score	>0.5 mg/dL	test en reference test: 48	effect size (include 95%Cl	
	cohort study	undergoing PCI		(44.2µmol/L) or 25%	hours	and p-value if available):	
		for STEMI, single	Comparator test:	increase in serum			
	Setting: in-	center	Marenzi risk score	creatinine within 48	For how many	AUC	
	and			hours of PCI	participants were no	Mehran: 0.57 (95% CI 0.52	
	outpatients	Exclusion			complete outcome data	- 0.62)	
		criteria:			available?	Marenzi: 0.57 (95% CI 0.51	
	Country: Italy	-			NR	- 0.62)	
	Conflicts of	N= 891			Reasons for incomplete		
	interest: not				outcome data described?		
	reported	Prevalence: 14%			NR		
		Mean age ± SD:					
		64 ± 13					
		Sex: 78% M					
Tziakas, 2013	Type of	Inclusion criteria:	Describe index test:	Describe reference test:	Time between the index	Outcome measures and	
	study ²⁰ :	Elective or	Tziakas score	>0.5 mg/dL or 25%	test en reference test: 48	effect size (include 95%Cl	
	cohort study	emergency PCI,		increase in serum	hours	and p-value if available):	
		single center		creatinine within 48			
	Setting: in-			hours of PCI	For how many	Calibration /	
	and	Exclusion			participants were no	discrimination:	
	outpatients	criteria:			complete outcome data	0.76	
		-			available?	p>0.05	
	Country:				NR		
	Greece	N= 688				External validation	
					Reasons for incomplete	Cohort 1: PCI patient same	
	Conflicts of	Incidence of			outcome data described?	single center	
	interest: not	events:			NR	N=200	

¹⁹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ²⁰ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

	reported	Derivation cohort: 10% Validation cohort: 14% Mean age ± SD: 64 ± 11 Sex: 74% M				Discrimination: 0.86 Calibration: NR Cohort 2: patients admitted for elective or emergency PCI, multiple centers (tertiary care) N=2689 Discrimination: 0.70 Calibration: p=0.18	
Tziakas, 2014	Type of study ²¹ : cohort study Setting: in- and outpatients Country: Greece Conflicts of interest: not reported	Inclusion criteria: PCI, elective or urgent, multiple centers Exclusion criteria: - N=2882 Prevalence: 16% Mean age ± SD: 61 ± 12 Sex: 70% M	Describe index test: Tziakas score	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 48 hours of PCI	Time between the index test en reference test: 48 hours For how many participants were no complete outcome data available? NR Reasons for incomplete outcome data described? NR	Outcome measures and effect size (include 95%Cl and p-value if available): AUC: 0.70 Risk score range associated with PC-AKI risk: ≤3: <20% >3: ≥20%	Internal validation only
Victor, 2014	Type of study ²² : cohort study Setting: in-	Inclusion criteria: patients with an indication for PCI, single center	Describe index test: "simple risk score for CIN"	Describe reference test: >0.5 mg/dL or 25% increase in serum creatinine within 48 hours of PCI	Time between the index test en reference test: 48 hours For how many	Outcome measures and effect size (include 95%Cl and p-value if available): Sens: 94%	

²¹ In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten (Lijmer et al., 1999) ²² In geval van een case-control design moeten de patiëntkarakteristieken per groep (cases en controls) worden uitgewerkt. NB; case control studies zullen de accuratesse overschatten

⁽Lijmer et al., 1999)

and		Exclusion		participants were no	Spec: 90%	
outp	patients	criteria:		complete outcome data		
		-		available?	External validation	
Cour	ntry: India			NR	N=300	
		N=900			Sens: 92%	
Conf	flicts of			Reasons for incomplete	Spec: 82%	
inter	rest: not	Incidence of		outcome data described?		
repo	orted	events:		NR		
		Derivation				
		cohort: 9.7%				
		Validation				
		cohort: 8.7%				
		Mean age ± SD:				
		57 v 10				
		Sex: 84% M				

Literature search description

Database	Search terms	Tota
	1 exp contrast media/ae or (contrast adj3 iodine).ti,ab. or (contrast adj3 media).ti,ab.	868
	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
	(537305)	
	3 1 and 2 (3895)	
	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
	ciaki).ti,ab. (1975)	
	5 3 or 4 (4504)	
	6 limit 5 to (yr="2000 -Current" and (dutch or english)) (2892)	
	7 risk assessment/mj or risk factors/mj or exp Renal Insufficiency/mj or Glomerular Filtration	
	Rate/ (35215)	
	8 (((kidney or renal) adj2 function) or (risk adj2 (assessment or factor* or scor*)) or egfr or	
	gfr or 'glomerular filtration rate').ti,ab. (559159)	
	9 exp contrast media/ad (14851) 10 7 or 8 (570621)	
	11 6 and 10 (1311)	
	12 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or	
	literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature	
	as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or	
	psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data	
	extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not	
	humans/)) (248785)	
	13 11 and 12 (75)	
	14 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or	
	randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii	
	or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or	
	multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or	
	doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not	
	(animals/ not humans/) (1510354)	
	15 11 and 14 (405)	
	16 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled	
	Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort	
	analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or	
	studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time	
	series analysis/ [Onder exp cohort studies/ of historically controlled study/ of interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en	
	retrospectieve studies] (2212779)	
	17 11 and 16 (574)	
	18 (recommend* or consensus*).ti. (47665)	
	19 guideline*.ab. /freq=2 (47817)	
	20 guideline*.ti. (54427)	
	21 Guideline/ or Practice Guideline/ or guidelines as topic/ or practice guidelines as topic/	
	22 or/18-21 (216370)	
	23 11 and 22 (50) 24 13 or 15 or 17 or 22 (811)	
	24 13 or 15 or 17 or 23 (811) 25 13 or 23 (114) – 112 uniek	
	26 15 not 25 (359) – 353 uniek	
	27 25 or 26 (473)	
	28 17 not 27 (338) – 328 uniek	

Literature search for tools to estimate risk of PC-AKI:

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. or	311
(OVID)	ESUR.ti,ab. (113073)	
1995-	2 exp *Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
now	(468614)	
English,	3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
Dutch	ciaki).ti,ab. (2004)	
Dutch	4 (1 and 2) or 3 (8499)	
	10 2 or 3 (468663)	
	11 8 and 10 (3)	
	12 limit 4 to (yr="1995 -Current" and (dutch or english)) (5270)	
	13 "Contrast Media"/ae [Adverse Effects] (8177) 14 "risk factor*".ab. /freq=3 (50816)	
	15 "Mass Screening"/ (86742)	
	16 "Risk Assessment"/ (192736)	
	17 (prediction or (risk adj3 (factor* or score* or marker*)) or screening).ti. (249759)	
	18 exp Questionnaires/ (343170)	
	19 (Questionnaire* or assessment*).ti. (220569)	
	20 Glomerular Filtration Rate/ or Creatinine/ or ("serum creatinine" or "glomerular	
	filltration rate*").ti,ab. (96312)	

21 14 or 15 or 16 or 17 or 18 or 19 (988425)
22 12 and 21 (645)
23 exp "Sensitivity and Specificity"/ or (Sensitiv* or Specific*).ti,ab. or (predict* or ROC- curve or receiver-operator*).ti,ab. or (likelihood or LR*).ti,ab. or exp Diagnostic Errors/ or (inter-observer or intra-observer or interobserver or intraobserver or validity or kappa or reliability).ti,ab. or reproducibility.ti,ab. or (test adj2 (re-test or retest)).ti,ab. or "Reproducibility of Results"/ or accuracy.ti,ab. or Diagnosis, Differential/ or Validation
Studies.pt. or *"Practice Guidelines as Topic"/ (4973682)
24 22 and 23 (323)
25 remove duplicates from 24 (311)

Appendices to Chapter 5

Evidence tables

No literature search was performed for this chapter. The working group did not expect to find evidence for this question, since the clinical question could not be answered in a controlled study. Furthermore, the recommendations typically apply for the Dutch healthcare system.

Search conditions

No literature search was performed for this chapter. The working group did not expect to find evidence for this question, since the clinical question could not be answered in a controlled study. Furthermore, the recommendations typically apply for the Dutch healthcare system.

Appendices to Chapter 6

Evidence tables

Table: Exclusion after	revision of full text
Author and year	Reason for exclusion
Akyuz. 2014	Patients with normal kidney function
Alessandri, 2014	Patients with normal kidney function
Cho, 2010	Does not fulfill selection criteria
Heguilen, 2013	Not using the most widely used PC-AKI definition of SC rise ≥25% or 44µmol/I
Кос, 2013	Patients with normal kidney function
Kong, 2012	Patients with normal kidney function
Kotlyar, 2005	Does not fulfill inclusion criteria (compares iv hydration with N-acetylcysteïne to hydration with placebo, not different hydration strategies)
Lawlor, 2007	Mixture of oral and intravenous hydration, compared to intravenous hydration alone
Mahmoodi, 2014	Patients with normal kidney function
Manari, 2014	The studied hydration infusion mixture is not used in Dutch clinical practice
Martin-Moreno, 2015	Patients with normal kidney function
Mueler, 2005	Does not fulfill inclusion criteria (no control group)
Pakfetrat, 2009	The studied hydration infusion mixture is not used in Dutch clinical practice
Taylor, 1998	Mixture of oral and intravenous hydration, compared to intravenous hydration alone
Thayssen, 2014	Patients with normal kidney function
Trivedi, 2003	Normal kidney function
Vashegani Ferahani,	The studied hydration infusion mixture is not used in Dutch clinical practice
2009	
Wrobel, 2014	Did not define CIN/CI-AKI/PC-AKI
Yeghanehkah, 2014	The studied hydration infusion mixture is not used in Dutch clinical practice

Evidence table

Research question

Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵ (unlikely/likely/un	Bias due to violation of intention to treat analysis? ⁶ (unlikely/likely/unclear)
	clear)	clear)	ear)	ear)	r)	clear)	
			Hydration versu	us no hydration			
Computer generated allocation sequence (stratified by hospital and renal function)	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Computer- generated using ALEA screening and enrolment application software.	Unlikely	Likely			Unlikely	Unlikely	Unlikely
			Oral hy	dration			
Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
	method of randomisation ¹	method of randomisation1inadequate concealment of allocation?2Computer generated allocation(unlikely/likely/un clear)Computer generated allocationUnlikelySequence (stratified by hospital and renal function)UnlikelyComputer- generated using ALEA screening and enrolment application software.UnlikelyNot decribed: "randomly assigned"UnlikelyNot decribed: "randomly assigned"Unlikely	method of randomisation1inadequate concealment of allocation?2inadequate blinding of participants to treatment allocation?3Computer generated allocationUnlikely/likely/un clear)(unlikely/likely/un clear)Computer generated allocation sequence (stratified by hospital and renal function)UnlikelyUnlikelyComputer- generated using ALEA screening and enrolment application software.UnlikelyLikelyNot decribed: "randomly assigned"UnlikelyUnlikelyUnlikelyUnlikelyUnlikely	method of randomisation1inadequate concealment of allocation?2inadequate 	method of randomisation1inadequate inadequate concealment of allocation?2inadequate blinding of participants to treatment allocation?3inadequate blinding of care providers to treatment allocation?3inadequate blinding of outcome assessors to treatment allocation?3(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/un clear)(unlikely/likely/uncl ear)(unlikely/likely/uncl ear)(unlikely/likely/uncl ear)Computer generated allocation sequence (stratified by hospital and and enrolment application software.UnlikelyUnlikelyUnlikelyUnlikelyLikely undikelyLikely unlikelyLikelyLikelyUnlikelyUnlikelyNot decribed: "randomly assigned"Unlikely unlikelyUnlikelyUnlikelyUnlikelyComputer generated and enrolment application software.UnlikelyUnlikelyUnlikelyUnlikelyNot decribed: "randomly assigned"UnlikelyUnlikelyUnlikelyUnlikelyUnlikelyComputer generated randomizationUnlikelyUnlikelyUnlikelyUnlikely	method of randomisation1inadequate concealment of allocation?2inadequate blinding of participants to treatment allocation?3inadequate blinding of care providers to treatment allocation?3inadequate blinding of outcome assessor to treatment allocation?3outcome reporting on basis of the results?4(unlikely/likely/un clear)(unlikely/likely/uncl clear)(unlikely/likely/uncl ear)(unlikely(unlikely(unlikely(unlikely(unlikelyComputer generated using and enrolment application software.UnlikelyUnlikelyUnlikelyUnlikelyUnlikelyUnlikelyUnlikelyNot decribed: "randomly assigned"UnlikelyUnlike	method of randomisation1inadequate concealment of allocation?2inadequate blinding of oparticipants to treatment allocation?3inadequate blinding of care providers to treatment allocation?3inadequate blinding of outcome assessors to treatment allocation?3outcome reporting on basis of the results?4to follow-up?5(unlikely/likely/un clear)(unlikely/likely/uncl clear)(unlikely/likely/uncl clear)(unlikely/likely/uncl ear)(unlikely/likely

Adolph, 2008	Computer- generated randomization schedule	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	
Boucek, 2013	Computer- generated randomization schedule with the use of numbered opaque envelopes containing identification of assigned medication	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Brar, 2008	Computer- generated randomization schedule	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Gomes, 2012	Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely	
Huber, 2016	Computer- generated randomization list	Unlikelu	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	
Manari, 2014	Computer generated balanced randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	
Ozcan, 2007	Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	
Ratcliffe, 2009	Not decribed: "randomization	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Unclear	

	block"								
Recio- Mayoral, 2007	Not decribed: "randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely	
		Sodium bicar	bonate short schedul			giography and/or percuta			
Briguori, 2007	Computer- generated randomization schedule	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Castini, 2008	Computer- generated randomization table	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	
Hafiz, 2012	Random allocation table	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Klima, 2012	Sealed envelopes	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Lee, 2011	Interactive web response system, computer generated randomization, stratified by participating center	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Maioli, 2008	Computerized open-label assignment in blinded envelopes used in a consecutive fashion	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	
Nieto- Rios, 2014	Sealed opaque envelopes (random numbers table)	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	

Shavit, 2009	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
2000		Sodium	bicarbonate versus sa	line: "other schedule	s" for coronary angiogra	aphy and/or percutaneou	us intervention	
Chong, 2015	Block randomisation, stratified by site, using aweb- randomisation system or back- up randomisation envelopes.	Unlikely	Likely	Unclear	Unlikely	Unlikely	Unlikely	Unlikely
Motohiro, 2011	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Tamura, 2009	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Turedi, 2016	Computer- based block randomization.	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
Ueda, 2011	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
				te short schedule ver		e for computed tomograp	· · · · · · · · · · · · · · · · · · ·	
Kooiman, 2014	Computer- generated allocation sequence	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
				Cor	trolled diuresis			
Brar, 2014	Computer- generated concealed	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely

	randomisation schedule							
Barbanti, 2015	Randomization based on computer generated codes	Unlikely	Likely	Likely	Unlikely	Unlikely	Unlikely	Unlikely
Briguori, 2011	Computer- generated randomisation list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Marenzi, 2012	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Qian, 2016	"randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Usmiani, 2015	"randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Usmiani, 2016	Randomly subdivided	Unlikely	Likely	Likely	Unlikely	Unlikely	Unclear	Unlikely
Visconti, 2016	Prospective, non- randomised study	Likely	Unclear	Unclear	Unclear	Unlikely	Unclear	Unclear

7. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

8. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

9. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

10. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

- 11. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 12. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1 This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Study	Study	Patient	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures	Comments
reference	characteristics	characteristics ²				and effect size ⁴	
			Hydration	versus no hydration			
Kooiman,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2014	randomized	1) adult patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	≥18 years with a			96 hours	(include 95%CI and	
		clinical suspicion of	Withholding hydration prior to	250mL iv 1.4% sodium bicarbonate		p-value if	Our results
	Setting:	a pulmonary	СТРА	1 hour before CTPA	Loss-to-	available):	suggest that
	emergency	embolis requiring			<u>follow-up</u> :		preventive
	patients,	computed			3/138 (2.2%)	CI-AKI	hydration could
	multiple	tomography-			2 lost to	(= creatinine	be safely withheld
	centers, both	pulmonary			follow-up	increase >25% /	in CKD patients
	in- and	angiography (CTPA)			1 died	>0.5mg/dL)	undergoing CTPA
	outpatients	chronic kidney				I: 6 (9%)	for suspected
		disease (CKD): eGFR				C: 5 (7%)	acute pulmonary
	Country: the	<60mL/min/1.73m ²			Incomplete	RR: 1.29, 95% CI:	embolism.
	Netherlands				<u>outcome</u>	0.41 - 4.03	
		Exclusion criteria:			<u>data</u> :		
	Source of	1) pregnancy			As above	None of the	
	funding: non-	previous contrast				patients developed	
	commercial	administration				a need for dialysis	
		within past 7 days					
		documented					
		allergy for					
		iodinated contrast					
		media					

Research question

	1					1	
		4) hemodynamic					
		instability (systolic					
		blood pressure					
		<100mmHg)					
		5) earlier					
		participation in					
		samen trial					
		N total at baseline:					
		Intervention: 67					
		Control: 71					
		Important					
		prognostic factors ² :					
		For example					
		age ± SD:					
		l: 70 ± 12					
		C: 71 ± 13					
		Sex:					
		I: 52% M					
		C: 48% M					
		eGFR ± SD:					
		I: 50 ± 16					
		C: 48 ± 15					
		Groups comparable					
		at baseline?					
		Yes					
Nijssen,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2017	randomized	1) eGFR: 45-59	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
(AMACING)	controlled trial	mL/min/1.73m ²	· · · · · · · · · · · · · · · · · · ·		2-6 days	(include 95%CI and	
, ,		combined with	Prophylactic hydration protocols	No prophylactic treatment.	,-	p-value if	'We found no
	Setting:	either diabetes, or	according to current guidelines:		Loss-to-	available):	prophylaxis to be
	elective	at least two			follow-up:		non-inferior and
L	0.000000	<u></u>			<u></u>		

	and the set state	Chandrand and the set in the set	1. 00/220		
patients, one	predefined risk	Standard protocol intravenous	I: 68/328	CI-AKI	cost-saving in
university	factors (age>75y;	0.9% NaCl 3–4 mL/kg per h during	C: 25/332	(25% or 44 µmol/L	preventing
hospital	anaemia defined as	4 h before and 4 h		within 2–6 days of	contrast-induced
	haematocrit values	after contrast administration; long	Incomplete	contrast exposure)	nephropathy
Country: the	<0.39L/L for men,	protocol intravenous	<u>outcome</u>	I:8 (2.7%)	compared with
Netherlands	and <0.36L/L for	0.9% NaCl 1 mL/kg per h during 12	<u>data</u> :	C: 8 (2.6%)	intravenous
	women;	h before and 12 h after	As above	P=0.417	hydration
Source of	<u>cardiovascular</u>	contrast administration.			according to
funding:	disease; non-			No hydration was	current clinical
Stichting de	steroidal anti-			cost-saving relative	practice
Weijerhorst	inflammatory drug;			to hydration.	guidelines.'
	or diuretic				
	nephrotoxic			No haemodialysis	
	medication).			or related deaths	
	<u>-</u>			occurred within	
	Exclusion criteria:			35 days.	
	1) Inability to				
	obtain informed				
	consent;				
	2) eGFR lower than				
	30mL per				
	min/1.73m ² ;				
	3) renal				
	-				
	replacement				
	therapy;				
	4)emergency				
	procedures;				
	5) intensive care				
	patients;				
	6) known inability				
	to perform primary				
	endpoint data				
	collection;				
	7) no referral to				
	prophylactic				
	hydration;				
	8) participation in				

							
		other RCT; and					
		isolation due to					
		infection control					
		N total at baseline:					
		Intervention: 328					
		(11: 328, 12: 296)					
		Control: 332					
		(C1: 332, C2: 307)					
		· · · ·					
		Important					
		prognostic factors ² :					
		For example					
		age ± SD:					
		l: 71.9 ± 9.3					
		C: 72.6 ± 9.3					
		Sex:					
		I: 59% M					
		C: 64% M					
		Baseline SCr:					
		<i>l:118.7±28</i> μmo1/L					
		C:117.7±25 μmo1/L					
		Groups comparable					
		at baseline? Yes					
	•		Oral	hydration			
Cho, 2010	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized	1) patients 18 years	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	hydration:
	controlled trial	or older with stable			72 hours	(include 95%CI and	
		serum creatinine				p-value if	Oral hydration
	Setting:	levels of at least	1) oral hydration with 500mL of	1) pretreatment with a 3mL/kg	Loss-to-	available):	with or without
	elective	1.1mg/dL or	water to be started 4 hours prior	bolus of intravenous saline	follow-up:		sodium
	patients, one	estimated	to contrast exposure and stopped	solution (154mEq/L) over 1 hour	Not reported	CIN	bicarbonate prior
	hospital	creatinine	2 hours prior to procedure	priori to contrast exposure		(= >25% increase in	to and following
		clearance less than	followed by oral hydration with	Intravenous infusion of 1mL/kg for	Incomplete	sCr from baseline	CAG is not

Country:	60mL/min	600mL water postprocedure	6 hours after procedure	outcome	or an absolute	inferioir to
United St	ates scheduled for			data:	increase of	intravenous
of Americ	a diagnostic, elective	2) oral hydration with 500mL of	2) pretreatment with a 3mL/kg	Not reported	0.5mg/dL from	hydration and
	angiography	water to be started 4 hours prior	bolus of intravenous sodium		baseline at 72	sodium
Source of		to procedure and stopped 2 hours	biacrbonate solution (154mEq/L)		hours following	bicarbonate with
funding: r	not <u>Exclusion criteria</u> :	prior to contrast exposure, with	over 1 hour priori to contrast		exposure to radio-	respect to CIN;
reported	1) serum creatinine	the addition of 3.9g (46.4mEq) of	exposure		contrast)	and to date, offers
	levels >8.0mg/dL	oral sodium bicarbonate to be	Intravenous infusion of 1mL/kg for		11: 1/22	an equivalent and
	2) change in serum	given 20 minutes prior to contrast	6 hours after procedure		12: 1/22	practical approach
	creatinine levels of	exposure followed by oral			C1: 6/27	in preventing a
	at least 0.5mg/dL	hydration with 600mL of water and			C2: 2/21	decline in renal
	during the previous	1.95g (30.4mEq) of oral sodium			p>0.05	functionafter
	24 hours	bicarbonate 2 hours and 4 hours				contrast exposure
	3) pre-existing	after the initial dose			There were no in-	without accuring
	dialysis				hospital mortalities	additional delay in
	4) multiple				during this study.	hospital days or
	myeloma or other					in-hospital
	myeloproliferative				Length of hospital	mortality,
	disease				stay did not differ	
	5) current				significantly	
	decompensated				between groups.	
	heart failure or					
	significant change					
	in NYHA					
	6) current					
	myocardial					
	infarction					
	symptomatic					
	hypokalaemia					
	8) uncontrolled					
	hypertension					
	9) exposure to					
	radiocontrast					
	within 7 days of					
	enrolment into this					
	study					
	10) emergency					

catheterisation		
11) allergy to		
radiographic		
contrast		
12) pregnancy		
13) administration		
of mannitol,		
feoldapam or NAC		
during the time of		
the study		
14) exacerbation of		
chronic obstructive		
pulmonary disease		
15) serum		
bicarbonate greater		
than 28eEw/L and		
sodium less than		
133mEq/L		
N total at baseline:		
Intervention: 43		
(11: 22, 12: 22)		
Control: 48		
(C1: 27, C2: 21)		
Important		
prognostic factors ² :		
For example		
age ± SD:		
<i>11: 81 ± 7</i>		
12: 79 ± 2		
<i>C1:</i> 77 ± 8		
<i>C2: 78 ± 9</i>		
Sex:		
I1: 45% M		
I2: 38% M		

		C1: 63% M C2: 52 Baseline SCr: I1: 1.38 I2: 1.31 C1: 1.38 C2: 1.41					
		Groups comparable at baseline? Yes					
2006	Type of study: randomized controlled trial Setting: elective patients, one university hospital Country: France Source of funding: non- commercial	Inclusion criteria: 1) patients referred for any radiological procedures necessitating a contrast medium injection and who had a baseline Cockcroft clearance between 15- 60ml/min 2) either chronic renal failure and on a kidney graft Exclusion criteria: 1) <18 years old 2) women of child- bearing age not using contraception or breast feeding 3) patients with heart failure and ejection fraction	Describe intervention (treatment/procedure/test): NaCl 1g/10kg/day per os for 2 days	Describe control (treatment/procedure/test): 0.9% saline iv 15ml/kg for 6 hours before the procedure	Length of follow-up: 48 hours Loss-to- follow-up: Not reported per group separately, in total 3/315 (1%) lost to follow-up Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (= increase in the baseline sCr concentration of at least 44µmol/L (0.5mg/dL) within 48 hours after the injection of contrast media) 1: 5/76 (7%) C: 4/77 (5%) p>0.05 None of the patients had fluid overload	Authors' conclusion: Oral saline hydration was as efficient as intravenous saline hydration for the prevention of CIN in patients with stage 3 renal diseases.
		<30% 4) uncontrolled					

r			I
	arterial		
	hypertension		
	5) obvious		
	extracellular		
	overhydration		
	6) respiratory		
	depression		
	7) known prior		
	intolerance to		
	theophylline or		
	furosemide		
	8) previous		
	exposure to		
	contrast media in		
	the 14 days before		
	randomization		
	9) unwilling or		
	unable to provide		
	informed consent		
	10) adequate time		
	prior to contrast		
	media injection was		
	not available to		
	perform the study		
	procedure		
	11) if sCr		
	measurements		
	varied by >10% in		
	the previous weeks		
	before referral		
	N total at baseline:		
	Intervention:		
	Control:		
	Important		
	prognostic factors ² :		
•			

		2) allergies to trial medication			coronary bypass and	P=0.61	chloride solution for volume
		infarction			emergency	C: 2.7%	sodium or sodium
		Exclusion criteria: 1) acute myocardial			2 patients had an	contrast axposure) I: 4.2%	use of either bicarbonate
	reported	Evolution aritoria:			3/145 (2%)	days 1 or 2 after	regardless of the
	funding: not	angiography			data:	between day 0 and	osmolar iodixanol
	Source of	coronary			outcome	25%above baseline	non-ionic, iso-
		interventional	administration	administration	Incomplete	(44µmol/L) or	after exposure to
	Germany	diagnostic or	and for 6 hours after contrast	and for 6 hours after contrast		>0.5mg/dL	low rate of CIN
	Country:	undergoing elective	1ml/kg body weight/hour during	1ml/kg body weight/hour during	follow-up)	concentration	homogenously
		(1.2mg/dL)	And	And	(refused	(= elevation of sCr	demonstrates a
	patients	106µmol/L	hours before	hours before	1 patient	CIN	exposure
	elective	greater than	2ml/kg body weight/hour for 2	2ml/kg body weight/hour for 2	follow-up:		radiocontrast
	Setting:	concentration	5% dextrose solution	dextrose solution	Loss-to-	available):	following
		serum creatinine	Sodium bicarbonate 154mEq/L in	Sodium chloride 154 mEq/L in 5%		p-value if	Renal Insufficiency
	controlled trial	years with baseline		· · · · · · · · · · · · · · · · · · ·	2 days	(include 95%CI and	
2008	randomized	1) patients >18	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
Adolph,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	1		L short schedule versus saline short sch	edule for coronary angiography and/or	percutaneous in	tervention	1
		at baseline? Yes					
		Groups comparable					
		$C: 33 \pm 11$					
		l: 38 ± 13 C: 33 ± 11					
		eGFR ± SD:					
		C:75 % M					
		I: 66% M					
		Sex:					
		0.0411					
		C: 64 ± 11					
		l: 63 ± 15					
		For example age ± SD:					

mediumwithin the	1 patient	not required	
last 7 days	refused		
4) thyroid	follow-up		
dysfunction			
5) pregnancy			
6) uncontrolled			
hypertension			
7) life-limiting			
concomitant			
disease			
8) pulmonary			
edema			
9) chronic dialysis			
10) administration			
of dopamine,			
mannitol,			
fenoldopam or NAC			
during the study			
N total at baseline:			
Intervention: 71			
Control: 74			
Important			
prognostic factors ² :			
For example			
age ± SD:			
1: 70 ± 8			
<i>C</i> : 73 ± 7			
Sex:			
I: 75% M			
C: 81% M			
sCr (mg/dL ± SD)			
l: 1.54 ± 0.51			
C: 1.57 ± 0.36			
0. 1.57 ± 0.50			

		Groups comparable at baseline? Yes					
Boucek, 2013	Type of study: RCT Setting: elective inpatients, one hospital Country: Czech Republic Source of funding: commercial		Describe intervention (treatment/procedure/test): 1.4% sodium bicarbonate in 5% glucose 3ml/kg/hour 1 hour before contrast administration (limited to a maximum of 330mL) 1mL/kg/hour 6 hours after contrast administration (limited to a maximum of 660mL)	Describe control (treatment/procedure/test): 0.9% saline in 5% glucose 3ml/kg/hour 1 hour before contrast administration (limited to a maximum of 330mL) 1mL/kg/hour 6 hours after contrast administration (limited to a maximum of 660mL)	Length of follow-up: 2 days – laboratory parameters 1 month – clinical parameters Loss-to- follow-up: Intervention: 3/61 (5%) Reasons not described Control: 3/59 (5%) Reasons not described Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (= sCr increase of ≥25% and/or 44µmol/L (0.5mg/dL) within 2 days foillowing administration of contrast) I: 7 (12%) C: 5 (9%) P=0.76 Incidence rate ratio: 1.35 (95% Cl: 0.37 – 5.41) No patients died or experienced severe kidney injury with need for acute dialysis treatment.	Authors' conclusion: In diabetic patients with renal function impairment sodium bicarbonate does not confer protection against contrast-induced nephropathy greater than sodium chloridebased hydration.
		procedure, 4) emergency type of procedure, acute kidney injury					

r			
	(serum creatinine		
	increase _50		
	mmol/L during the		
	previous		
	24-h period),		
	5) volume overload		
	with left ventricular		
	failure,		
	6) uncontrolled		
	hypertension		
	(systolic BP _180 or		
	diastolic BP		
	_110 mmHg),		
	7) hemodynamic		
	instability (systolic		
	BP <90 and		
	diastolic BP <50		
	mmHg),		
	8) contrast use in		
	the previous 48-h		
	period,		
	9) multiple		
	myeloma,		
	10) pregnancy or		
	breastfeeding		
	11) pre-planned use		
	of any other		
	measure for CIN		
	prevention		
	apart from the NaCl		
	or NaHCO3		
	infusions		
	N total at baseline:		
	Intervention: 61		
	Control: 59		

		Important prognostic factors ² : For example age ± SD:					
		l: 63 ± 11 C: 67 ± 10					
		Sex: I: 75% M C: 75% M					
		eGFR (mL/min/1.73m ²) ± SD I: 44 ± 19 C: 25 ± 17					
		C: 25 ± 17 Groups comparable at baseline? Yes					
Brar, 2008	Type of study: randomized controlled trial	Inclusion criteria: 1) an estimated glomerular	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	<u>Length of</u> <u>follow-up</u> : 2-3 days for	Outcome measures and effect size (include 95%Cl and	Authors' conclusion:
	Setting: elective patients, one	filtration rate (GFR) of 60 mL/min per 1.73m2 or less, 2) age 18	1.4% sodium bicarbonate iv infusion Infusion was begun 1 hour prior to the start of contrast	0.9% saline iv infusion Infusion was begun 1	laboratory parameters 6 months for clinical	p-value if available):	The results of this study do not suggest that hydration with
	hospital	years or older, 3) at least 1 of the	administration at3mL/kg for1hour, decreased	hour prior to the start of contrast administration	effects	≥25% reduction in estimated eGFR	sodium bicarbonate
	Country: United States of America	follwing: -diabetes mellitus, -history of	to 1.5 mL/kg per hour during the procedure and for 4 hours following	at3mL/kg for1hour, decreased to 1.5 mL/kg per hour during the procedure	Loss-to- follow-up: Intervention:	I: 21/158 (13% C: 24/165 (15%) Absolute	is superior to hydration with sodium chloride
	Source of funding:	congestive heart failure, -hypertension	completion of theprocedure.Forpatientsweighing	and for 4 hours following completion of	17 (10%) Excluded 1 Did not	difference: 1.3, 95% CI: -6.3 to 8.8, p=0.75	for the prevention of contrast medium–induced
	commercial	(140/90 mm Hg treatment with an antihypertensive	more than 100 kg, the bolus and infusion rate were limited to those used for	theprocedure.Forpatientsweighing more than 100 kg, the bolus and infusion	undergo coronary angiography	Serum creatinine >25% or >0.5mg/dL	nephropathy in patients with moderate to

medication),	patients weighing100kg	rate were limited to those used for	16 Did not	increase	severe chronic
-age older than 75	1	patients weighing100kg	have	I: 26/158 (17%)	kidney disease
years		patients treighting20018	estimated	C: 30/165 (18%)	who are
yeare			GFR data	Absolute	undergoing
Exclusion criteria:			1-4 d after	difference: 1.7,	coronary
1) inability to			procedure	95% CI: -6.5 to	angiography.
obtain consent, 2)			p	10.0, p=0.78	
receipt of a sodium			Control:	10.0, p 0.70	
bicarbonate			13 (7%)	30-day mortality	
infusion prior to			Excluded	I: 3/175 (2%)	
randomization,			2 Did not	C: 3/178 (2%)	
3) emergency			undergo	p>0.05	
cardiac			coronary		
catheterization,			angiography	6-month mortality	
4) intra-aortic			11 Did not	1: 34%	
balloon			have	C: 2%	
counterpulsation,			estimated	P=0.54	
5) dialysis,			GFR data		
6) exposure to			1-4 d after	6-month start of	
radiographic			procedure	dialysis	
contrast media				I: 2/175 (1%)	
within the			Incomplete	C: 4/178 (2%)	
preceding 2 days,			outcome	P-value not	
7) allergy to			data:	reported	
radiographic			As above for		
contrast media,			laboratory		
8) acutely			paramters.		
decompensated			All patients		
congestive heart			were		
failure,			followed up		
9) severe valvular			for clinical		
, abnormality (eg,			events.		
severe aortic					
stenosis or					
mitral					
regurgitation),					
10) single					

	T	_			1		· · · · · · · · · · · · · · · · · · ·
		functioning					
		kidney,					
		11) history of					
		kidney or heart					
		transplantation,					
		12) change in					
		estimated GFR of					
		7.5% or more per					
		day or a cumulative					
		change of15%or					
		more over the prior					
		2 or more days					
		N total at baseline:					
		Intervention: 175					
		Control: 178					
		Important					
		prognostic factors ² :					
		For example					
		age (IQR range)					
		I: 71 (65-75)					
		C: 71 (65-76)					
		Sex:					
		I: 65% M					
		C: 62% M					
		Groups comparable					
		at baseline? Yes					
Gomes,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2012	randomized	1) patients at	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	moderate to high			48 hours	(include 95%CI and	
		risk for developing				p-value if	Hydration with
	Setting:	CIN who were			Loss-to-	available):	sodium
	elective	referred for elective	154 mEq/l of sodium bicarbonate	0.9% saline infusion	follow-up:		bicarbonate was
	patients, 6	coronary	in 5% dextrose and H ₂ O	3 mL/ kg/ h for 1 hour immediately	Not reported	CIN	not superior to
L	1		2			l	l

difference	angiography or PCI	3 mL/ kg/ h for 1 hour immediately	before contrast injection		(=an increase in	saline to prevent
centres	at 6 centers	before contrast injection	same fluid at a rate of 1 mL/kg/h	Incomplete	serum creatinine ≥	contrast media
centres	2) serum creatinine	same fluid at a rate of 1 mL/kg/h	during contrast exposure and for 6	outcome	0.5 mg/dL 48 hours	induced
Country: Brazi		during contrast exposure and for 6	hours after the procedure		after exposure to	nephropathy in
Country. Brazi	glomerular	hours after the procedure	nours after the procedure	<u>data</u> :	contrast medium)	patients at risk
Source of	filtration rate (GFR)	nours after the procedure		Not reported		
					I: 9/150 (6%)	undergoing
funding: none	<50 mL/min				C: 9/151 (6%)	cardiac
reported					P=0.97	catheterization.
	Exclusion criteria:					
	1) age <18 years,				Dialysis:	
	2) use of				I: 0%	
	radiographic				C: 0%	
	contrast media				P=1.00	
	during the last 21					
	days,				Death:	
	3) history of				I: 3%	
	dialysis,				C: 5%	
	4) cardiac				P=0.81	
	insufficiency class					
	III-IV NYHA,					
	5) emergency					
	procedures					
	<u>N total at baseline</u> :					
	Intervention: 150					
	Control: 151					
	Important					
	prognostic factors ² :					
	For example					
	age ± SD:					
	l: 64 ± 12					
	C: 65 ± 12					
	Sex:					
	I: 69% M					
	C: 75% M					

	eGFR ± SD I: 51 ± 13 C: 52 ± 13					
	Groups comparable at baseline? Yes					
Huber, 2016 Type of study: randomized controlled Setting: single- center university hospital Country: Germany Source of funding: institutional support	Inclusion criteria: 1) >18 years; 2) increased risk of CIN undergoing administration of CM. High risk was defined by a serum creatinine level ≥1.1 or ≥0.8 mg/dL plus an additional risk factor like diabetes mellitus, renal failure in past medical history, or nephrotoxic medication (aminoglycoside, vancomycin, amphotericin B, and diuretic). Exclusion criteria: 1) pre-existing renal replacement therapy; 2) unstable serum creatinine levels (difference of more than _0.4 mg/dL	Describe intervention (treatment/procedure/test): Group B received bicarbonate infusion with 200mg theophylline.	Describe control (treatment/procedure/test): Control group S received sodium chloride infusion with 200mg theophylline.	Length of follow-up: 48h after CM Loss-to- follow-up: 1:14/91 C: 14/94 Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN as a raise in serum creatinine of _25% or _0.5 mg/dL within 48 h after contrast application l: 1/74 (1.4%) C: 7/78 (9%) P=0.039 Dialysis: l: 9% C: 17% P=0.189	Authors' conclusion: 'In patients at increased risk of CIN receiving prophylactic theophylline, hydration with sodium bicarbonate reduces contrast- induced renal impairment compared to hydration with saline.'

	-		
within 3			
days before			
contrast			
application);			
3) contraindi-			
cations for			
theophylline			
or sodium			
bicarbonate			
(allergies,			
tachycardia,			
alkalosis,			
and hypokalemia);			
and;			
4) additional			
interventions that			
might			
influence renal			
function.			
Important			
prognostic factors ² :			
For example			
age ± SD:			
<i>I: 64.4 ± 15.7</i>			
C: 66.1 ±13.3			
Sex:			
I: 59.5% M			
С: 66.7% М			
Baseline SCr:			
l:1.25± 0.69 mg/dL			
C:1.38± 0.65 mg/dL			
Groups comparable			
at baseline? Yes			

Manari,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2014	randomized	1) Patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
-	controlled	with STEMI within		(,	3 days –	(include 95%CI and	
		12 h from symptom	11:	C1:	laboratory	p-value if	In patients with
	Setting:	onset referred	sodium bicarbonate solution 1	Intravenous normal saline (0.9%)	parameters	available):	STEMI undergoing
	emergency	for primary	ml/kg of body weight per hour for	at a rate of 1 ml/kg of body	12 months –		PPCI, highvolume
	patients,	angioplasty	12 h	weight per hour for 12 h	clinical	sCr increase ≥25%	hydration with
	multicentre	2) age at least 18			events	compared to	normal saline or
	trial	years	12:	C2:		baseline	sodium
		3) chest pain lasting	3 ml/kg of body weight per hour	normal saline at a	Loss-to-	I1: 24 (16%)	bicarbonate
	Country: Italy	for at least 30 min	for 1 h, followed by	rate of 3 ml/kg of body weight per	follow-up:	I2: 27 (18%)	administrated at
		associated with	1 ml/kg of body weight per hour	hour for 1 h followed by	Not reported	C1: 29 (19%)	the time of
	Source of	STsegment	for 11 h	1 ml/kg of body weight per hour		C2: 27 (19%)	contrast media
	funding: not	elevation of 0.2mV		for 11 h	Incomplete	P=0.92	administration
	reported	or more in at least			outcome		was not
		two			<u>data</u> :	sCr increase ≥0.5	associated with
		contiguous leads or			Not reported	mg/dL from	any significant
		new left bundle-				baseline	advantage in
		branch block				l1: 5 (3%)	terms
						12: 3 (3%)	of CI-AKI
		Exclusion criteria:				C1: 7 (5%)	prevention.
		1) the concomitant				C2: 8 (6%)	
		detection of				P=0.51	
		mechanical					
		complications,				Mortality did not	
		2) previous				differ at 30 days	
		peritoneal or				and at 12 months	
		hemodialysis				(data not shown).	
		treatment, 3) the					
		presence of					
		postanoxic coma					
		4) pregnancy					
		<u>N total at baseline</u> :					
		Intervention 1: 145					
		Intervention 2: 154					
		Control 1: 142					

		Control 2: 151					
		CONTOL 2. 151					
		Important					
		prognostic factors ² :					
		For example					
		age ± SD:					
		11: 64 ± 13					
		12: 65 ± 13					
		C1: 65 ± 13					
		C2: 65 ± 12					
		Sex:					
		l1: 72% M					
		I2: 75% M					
		C1: 75% M					
		С2: 77% М					
		eGFR ml/min					
		11: 80 ± 26					
		12: 82 ± 24					
		C1: 81 ± 23					
		C2: 82 ± 25					
		Groups comparable					
		at baseline? Yes					
Ozcan,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2007	randomized	patients who were	(treatment/procedure/test):	(treatment/procedure/test):	<u>follow-up</u> :	and effect size	conclusion
	controlled trial	scheduled			48 hours	(include 95%Cl and	
		for coronary	1.4% sodium bicarbonate	0.9% saline		p-value if	Hydration with
	Setting:	angiography or	lv fluid (1 mL/kg/h,	lv fluid (1 mL/kg/h,	Loss-to-	available):	sodium
	elective	percutaneous	upper limit 100 mL/h) for 6 hours	upper limit 100 mL/h) for 6 hours	follow-up:		bicarbonate
	patients	coronary	before and 6 hours after the	before and 6 hours after the	Not reported	CIN	provides better
	Country	intervention	procedure	procedure		(=an increase in	protection against
	Country:	and had a baseline			Incomplete	serum creatinine	CIN than the
	Turkey	creatinine level			outcome	N25% or 0.5 mg/dL	sodium chloride
	Source of	N1.2 mg/dL			<u>data</u> :	after 48 hours)	infusion does
	Source of	1			Not reported	I: 12/88	alone.

r	1	1	
funding: not	Exclusion criteria:		C: 4/88
reported	1) uncontrolled		P=0.043
	hypertension		RR (adjusted): 0.29
	(systolic and		95% CI: 0.09 – 0.96
	diastolic blood		
	pressure N160 mm		
	Hg and N110 mm		
	Hg, respectively),		
	2) emergency		
	catheterization,		
	3) recent exposure		
	to radiocontrast		
	medium within 2		
	days,		
	4) volume overload,		
	5) serum creatinine		
	levels >4 mg/dL		
	N total at baseline:		
	Intervention: 88		
	Control: 88		
	Important_		
	prognostic factors ² :		
	For example		
	age median		
	(minimum –		
	maximum)		
	1: 68 (43-86)		
	<i>C: 70 (40-84)</i>		
	Sex:		
	I: 73% M		
	C: 75% M		
	Creatinine		
	clearance (mL/min)		

	I: 53 (21 – 81) C: 50 (22-101) Groups comparable at baseline? Yes					
Ratcliffe, 2009 Type of stud randomized controlled t Setting: elective patients, 1 center Country: United State of America Source of funding: no reported	 ambulatory or hospitalized patients who were scheduled for invasive coronary angiography or percutaneous coronary intervention for the evaluation and treatment of coronary artery disease 	Describe intervention (treatment/procedure/test): Iv 0.9% NaHCO3 hydration at an infusion rate of 3 mL/kg/h for 1 h before contrast, and continued at 1 mL/kg/h during the procedure and for 6 h following contrast exposure	Describe control (treatment/procedure/test): Iv 0.9% saline hydration at an infusion rate of 3 mL/kg/h for 1 h before contrast, and continued at 1 mL/kg/h during the procedure and for 6 h following contrast exposure	Length of follow-up: 72 hours Loss-to- follow-up: Intervention: 15/30 (50%) Reasons: 11 lack of complete follow-up 4 other reasons Control: 10/29 (30%) 8 lack of complete follow-up 2 other reasons <u>Incomplete</u> outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase of greater than 25% in serum creatinine concentration from baseline to 72 h after administration of the contrast media) l: 2/19 (11%) C: 1/15 (7%) p>0.05	Authors' conclusion: CIN in high-risk patients may be effectively minimized solely through the use of an aggressive hydration protocol and an iso- osmolar contrast agent. The addition of NaHCO3 and/or NAC did not have an effect on the incidence of CIN.

in women) or		
reduced calculated		
creatinine		
clearance (less than		
1.002 mL/s) using		
the		
Cockcroft-Gault		
formula, and/or		
diabetes mellitus		
on oral antiglycemic		
or insulin therapy		
Exclusion criteria:		
1) pregnancy or		
lactation; 2) acute		
myocardial		
infarction;		
3) clinical signs of		
heart failure (or		
documented		
ejection fraction of		
less than 35%);		
4) cardiogenic		
shock; 5)		
hypertrophic or		
restrictive		
cardiomyopathy;		
6) contrast medium		
exposure within		
one week before		
the procedure;		
7) previous serious		
reactions to		
contrast medium;		
8) renal		
transplantation;		
dialysis; severe		
	1	

	1				r	1	1
		comorbid illness;					
		9) use of dopamine,					
		mannitol or					
		fenoldopam; 10)					
		newly discovered					
		uncontrolled					
		diabetes mellitus;					
		11) the inability to					
		obtain informed					
		consent or follow-					
		up					
		<u>N total at baseline</u> :					
		Intervention:					
		Control:					
		Important 2					
		prognostic factors ² :					
		For example					
		age ± SD:					
		l: 67 ± 11					
		C: 64 ± 10					
		Sex:					
		I: 58% M					
		C: 60% M					
		Groups comparable					
		at baseline? Yes					
Recio-	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
Mayoral,	randomized	1) acute coronary	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
2007	controlled trial	syndrome (ACS)			3 days	(include 95%CI and	
		patients who were				p-value if	Rapid intravenous
	Setting:	admitted to our	Active prophylactic treatment of	Standard treatment:	Loss-to-	available):	hydration with
	emergency	coronary care unit	PCI:	perfusion of isotonic saline (0.9%)	follow-up:		sodium
	patients, one	patients with	Intravenous bolus of 5 ml/kg/h of	at rate of 1 ml/kg/h for 12 h after	Not reported	CIN	bicarbonate plus
	hospital	myocardial	alkaline saline solution with 154	PCI plus 2 doses of 600 mg N-AC		(=an absolute	N-AC before

		infarction treated	mEq/I of sodium bicarbonate in 5%	orally the next day	Incomplete	increase in SCr	contrast injection
c	Country:	with primary PCI or	glucose and H2O (adding 77 ml of		outcome	concentration	is effective and
ι ι	United	rescue PCI, as well	1,000 mEq/l sodium bicarbonate to		data:	of 0.5 mg/dl or	safe in
к	Kingdom	as patients with	433 ml of 5% glucose in H2O) plus		Not reported	more from baseline	the prevention of
		high-risk non-ST-	2,400 mg of N-AC in the same		-	value in the 3 days	CIN in patients
S	Source of	segment elevation	solution over 1 hour the bolus was			after	undergoing
f	funding: not	ACS needing urgent	administered			PCI)	emergency PCI.
r	reported	revascularization	in the 60 min preceding contrast			I: 1/55 (2%)	
			injection			C: 12/55 (22%)	
		Exclusion criteria:	Afterward, patients received fluid			Odds ratio: 0.065	
		1) end-stage renal	therapy, without N-AC, at 1.5			(95% CI: 0.008 –	
		failure on dialysis,	ml/kg/h perfusion rate in the 12 h			0.521, p=0.01)	
		2) uncontrolled	after the procedure plus 2 doses of				
		hypertension	600 mg N-AC orally the next day			Acute anuric renal	
		(systolic blood				failure	
		pressure				I: 1/55 (2%)	
		>160 mm Hg and/or				C: 7/55 (13%)	
		diastolic blood				P=0.032	
		pressure >100 mm					
		Hg)					
		3) signs of cardiac					
		failure not					
		responding to					
		medical treatment,					
		4) known severe					
		aortic valve stenosis					
		(area >1.0 cm2),					
		5) allergy to iodated					
		contrast or NAC 6)					
		pregnancy					
		N total at bacalize:					
		<u>N total at baseline</u> : Intervention: 56					
		Control: 55					
		Important					
		prognostic factors ² :					
						1	

	1						 1
		For example					
		age ± SD:					
		I: 65 ± 10					
		C: 64 ± 9					
		Sex:					
		I: 68% M					
		C: 71% M					
		Glomerular					
		filtration rate					
		(mL/min)					
		I: 75 ± 21					
		C: 74 ± 20					
		Groups comparable					
		at baseline? Yes					
		Sodium bicarbonate	short schedule versus saline long sche	dule for coronary angiography and/or	percutaneous int	ervention	
Briguori,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2007	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	chronic kidney			48 hours for	(include 95%CI and	
		disease who	154 mEq/L sodium bicarbonate in	Isotonic saline (0.90%) was given	laboratory	p-value if	The strategy of
	Setting:	underwent	dextrose and H2O,.	intravenously at a rate of 1 mL/kg	parameters	available):	volume
	elective	coronary and/or	The initial intravenous bolus was 3	body weight per hour	5 days for		supplementation
	patients, one	peripheral	mL/kg/h for 1 hour immediately	(0.5 mL/kg for patients with left	clnical events	CIN	by sodium
	hospital	angiography and/or	before contrast injection. After	ventricular ejection fraction _40%)		(=increase _25% of	bicarbonate plus
		angioplasty	this, patients received the same	for 12 hours before and 12 hours	Loss-to-	creatinine	NAC seems to be
	Country: Italy	2) 18 years of age	fluid at a rate of 1 mL/kg/h during	after administration of the contrast	follow-up:	concentration)	superior to the
		3) stable serum	contrast exposure and for 6 hours	agent.	Intervention:	I: 2/108 (2%)	combination of
	Source of	creatinine	after the procedure.		9/117 (8%)	C: 11/111 (10%)	normal saline with
	funding: not	concentration >2.0		NAC orally at a dose of 1200 mg	8 had no	P=0.02	NAC alone or with
	reported	mg/dL and/or or an	NAC orally at a dose of 1200 mg	twice daily on the day before and	follow-up sCr		the addition of
		estimated	twice daily on the day before and	the day of administration of the	value	Renal failure	ascorbic acid in
		glomerular	the day of administration of the	contrast agent (total of 2 days).	1 had no	requiring	preventing CIN in
		filtration rate <40	contrast agent (total of 2 days).		contrast	temporary dialysis:	patients at
		mL/ min/1.73 m ²			exposure	I: 1/108 (1%)	medium to high
		-				C: 1/111 (1%)	risk.

		-			
	Exclusion criteria:		Control:	p-value not	
	1) serum creatinine		7/118(6%)	reported	
	levels >8 mg/dL,		7 had no		
	2) a history of		follow-up sCr		
	dialysis,		value		
	3) multiple				
	myeloma, 4)		Incomplete		
	pulmonary edema,		outcome		
	4) acute myocardial		data:		
	infarction,		As above		
	5) recent exposure				
	to radiographic				
	contrast within 2				
	days of the study,				
	6) pregnancy,				
	7) administration of				
	theophylline,				
	dopamine,				
	mannitol, or				
	fenoldopam				
	N total at baseline:				
	Intervention: 111				
	Control: 108				
	Important				
	prognostic factors ² :				
	For example				
	age ± SD:				
	<i>I: 70 ± 9</i>				
	C: 71 ± 9				
	Sex:				
	I: 88% M				
	C: 81% M				
	Groups comparable				
L I	or oups comparable				

		at baseline? Yes					
Castini, 2008	Type of study: randomized controlled trial Setting: one hospital Country: Italy Source of funding: not reported	Yes Inclusion criteria: 1) patients undergoing coronary angiography and/or percutaneous coronary intervention 2) aged 18 years or older with stable serum creatinine levels ≥1.2 mg/dL Exclusion criteria: 1) serum creatinine levels >4 mg/dL, 2) a history of dialysis, 3) multiple myeloma,	Describe intervention (treatment/procedure/test): 154 mL of 1000 mEq/L SB added to 846 mL of 5% dextrose in H2O. The initial intravenous bolus was 3 mL/kg for 1 hour immediately before contrast injection. Thereafter, patients received the same fluid at a rate of 1 mL/kg per hour during contrast exposure and for 6 hours after the procedure.	Describe control (treatment/procedure/test): saline (0.9%) given intravenously at a rate of 1 mL/kg body weight per hour for 12 hours before and 12 hours after administration of the contrast agent	Length of follow-up: 5 days Loss-to- follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN1 (=an increase in serum creatinine concentration≥25% over the baseline value in any of the 3 predefined time- points: 24 hours, 48 hours and 5 days) I: 7 (14%) C: 7 (14%) P>0.05	Authors' conclusion: Our findings suggest that neither the addition of NAC nor the administration of SB add further benefit in CIN prevention, compared to standard hydration with isotonic saline infusion.
		 4) pulmonary edema, 5) cardiogenic shock, 6) acute myocardial infarction, 7) emergency catheterization, 8) recent exposure to radiographic contrast media within 7 days of the study, 9) allergy to iodinate contrast media or NAC, 				CIN2 (=the rate of an absolute increase in serum creatinine concentration ≥0.5 mg/dL at the same time-points) I: 6 (12%) C: 4 (8%) p>0.05 No patients required dialysis.	

	1	1				1	
		10) previous					
		enrollment in the					
		same or other					
		protocols, 11)					
		pregnancy,					
		12) administration					
		of theophylline,					
		mannitol,					
		dopamine,					
		dobutamine,					
		nonsteroidal anti-					
		inflammatory					
		drugs, or					
		fenoldopam.					
		renoraopann					
		N total at baseline:					
		Intervention: 52					
		Control: 51					
		<u>Important</u>					
		prognostic factors ² :					
		For example					
		age ± SD:					
		l: 70 ± 8					
		C: 73 ± 8					
		Sex:					
		I: 85% M					
		C: 84% M					
		Groups comparable					
		at baseline? Yes					
Hafiz, 2012	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	coclusion:
	controlled trial	undergoing elective		· · · · · · · · · · · · · · · · · · ·	48 hours	(include 95%CI and	
		coronary and	dextrose 5% in water containing	intravenous 0.9% normal saline		p-value if	Incidence of CI-
	Setting:	peripheral	154 mEq/L of NaHCO3 with or	with or without NAC	Loss-to-	available):	AKI was no
	0.	p = p = o = o					

elective	angiography and	without NAC		follow-up:		different in the
patients, two	intervention.		NAC was used in 50% of patients in	Not reported	CI-AKI	NaHCO3 group
tertiary	2) serum creatinine	NAC was used in 50% of patients in	both study arms in a similarly		(=increase in serum	compared to
hospitals	>1.6 mg/dl in non-	both study arms in a similarly	randomized fashion as above;	Incomplete	creatinine	saline group, and
	diabetics and >1.4	randomized fashion as above;	1,200 mg was administered orally	outcome	concentration of	NAC did not
Country:	mg/dl in diabetics	1,200 mg was administered orally	2–12 hr before the procedure	data:	either >25% or >0.5	reduce CI-AKI in
, United states	or an estimated	2–12 hr before the procedure	followed by another 1,200 mg oral	Not reported	mg/dl at 48 hr after	the two study
of america	glomerular	followed by another 1,200 mg oral	dose 6–12 hr after the procedure		the procedure)	arms.
	filtration rate	dose 6–12 hr after the procedure			I: 12%	
Source of	(eGFR) of <50				C: 9%	
funding: not	ml/min/1.73 m2,				p>0.05	
reported	calculated by the					
	Modification of Diet				There were no	
	in Renal Disease				deaths or major	
	(MDRD) formula				adverse effects	
	3) age >18 years				noted in our	
					patient population	
	Exclusion criteria:				during	
	were on dialysis;				the study period.	
	(2) had unstable					
	renal function					
	(defined as change					
	in serum creatinine					
	of					
	>0.4 mg/dl within					
	48 hr prior to the					
	index procedure),					
	(3) had pulmonary					
	edema,					
	(4) had serum					
	bicarbonate level					
	>34 mmol/L;					
	(5) received					
	fenoldapam,					
	mannitol,					
	dopamine, or NAC					
	within 48 hr prior to					

					r		1
		the index					
		procedure;					
		(6) were in					
		cardiogenic shock,					
		(7) were allergic to					
		contrast media,					
		(8) were pregnant,					
		(9) were unable to					
		provide informed					
		consent.					
		N total at baseline:					
		Intervention: 159					
		Control: 161					
		Important [Variable]					
		prognostic factors ² :					
		For example					
		age (IQR):					
		I: 74 (65-80)					
		C: 73 (63-80)					
		Sex:					
		I: 56% M					
		C: 57% M					
		eGFR					
		I: 42 (32-51)					
		C: 41 (33-50)					
		Groups comparable					
		at baseline? Yes					
Klima, 2012	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized	All patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	admitted with renal			48 hours	(include 95%CI and	
		dysfunction {actual	The initial intravenous bolus was 3	The infusion of 0.9% sodium		p-value if	Volume
	Setting:	serum creatinine	mL/kg/h of 166 mEq/L sodium	chloride was administered at a	Loss-to-	available):	supplementation

e	elective	level above the	bicarbonate for 1 h immediately	continuous rate of 1 mL/kg/h,	follow-up:		with 24 h sodium
r F	patients,	upper limit of	before radiocontrast injection.	beginning from 8 p.m. on the day	Intervention:	CIN	chloride 0.9% is
r	multi-center	normal of the	Following this, patients received	before the procedure and for at	6/93 (6%)	(=an increase of	superior to
t	trial	serum creatinine	the same fluid at a rate of 1	least 12h after the procedure.	5 received no	≥25% or an	sodium
		(0.93 mmol/L for	mL/kg/h during the contrast		radiocontrast	increase of ≥44	bicarbonate for
0	Country:	women and .117	exposure and for 6 h after the		1 refused	μmol/L in the	the prevention of
S	Switzerland	mmol/L for men) or	procedure.		participation	baseline serum	CIN.
		estimated				creatinine	
S	Source of	glomerular			Control:	concentration	
f	funding:	filtration rate			4/93 (4%)	within 48 h)	
c	commercial	60, (eGFR)			4 received no	I: 9%	
a	and non-	mL/min/1.73 m2			radiocontrast	C:1%	
c	commerzial	[eGFR calculated				P=0.02	
		using the			Incomplete		
		abbreviated			outcome	No patient	
		Modification of Diet			<u>data</u> :	experienced a	
		in Renal Disease			As above	serious adverse	
		(MDRD) study				event related to	
		equation16]}				the infusion (death,	
		scheduled to				intensive care unit	
		undergo an intra-				admission). Also,	
		arterial or				no patient required	
		intravenous				intravenous	
		radiographic				diuretics or nitrates	
		contrast procedure				due to pulmonary	
		on the next day				congestion.	
		Exclusion criteria:					
		1) age ≥18 years,					
		2) pre-existing					
		dialysis, allergy to					
		radiographic					
		contrast,					
		3) pregnancy,					
		4) severe heart					
		failure (NYHA					
		functional class III					

r		1			1	1	
		and IV),					
		5) N-acetylcysteine					
		≤24 h before					
		contrast,					
		6) clinical condition					
		requiring					
		continuous fluid					
		therapy, e.g. severe					
		sepsis					
		N total at baseline:					
		Intervention: 87					
		Control: 89					
		Important					
		prognostic factors ² :					
		For example					
		age median (IQR):					
		l: 78 (70-82)					
		C: 75 (70-82)					
		Sex:					
		I: 66% M					
		C: 62% M					
		eGFR ± SD					
		l: 43 ± 11					
		C: 43 ± 12					
		Groups comparable					
		at baseline? Yes					
Lee, 2011	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
-	randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	undergoing			48 hours for	(include 95%CI and	
		coronary or			laboratory	p-value if	In conclusion,
	Setting:	endovascular	Sodium bicarbonate infusion (154	0.9% sodium chloride 1 ml/kg/hour	parameters	available):	hydration with
	elective	angiography or	mEq/L in dextrose and water) was	for 12 hours before and after the	6 months for		sodium
L	1		,, - , · · ·		1	1	

pa	atients,	intervention	begun 1 hour before the start of	procedure	clinical	CIN	bicarbonate is not
m	ulticentre	2) serum creatinine	contrast injection, starting at 3		parameters	(=a ≥25% increase	superior to
tri	ial academic	≥1.1 mg/dl,	ml/kg/hour and decreasing to 1	All patients received NAC 1,200 mg		in serum creatinine	hydration with
hc	ospitals	estimated	ml/ kg/hour during the procedure	2 times/day for 2 days starting the	Loss-to-	concentration	sodium chloride in
		glomerular	and for 6 hours after completion of	day before the index procedure	follow-up:	or a ≥0.5 mg/dl	preventing CIN in
Co	ountry:	filtration rate	the procedure		Intervention:	absolute increase	patients with
Кс	orea	(eGFR) ≤60			5/193 (3%)	in serum creatinine	diabetic
		ml/min/1.73 m ² ,			All had no	from baseline	nephropathy
So	ource of	age ≥18 years,	All patients received NAC 1,200 mg		laboratory	within 48 hours	undergoing
fu	inding: not	4) diagnosis with	2 times/day for 2 days starting the		data	after contrast	coronary or
re	eported	diabetes mellitus	day before the index procedure			exposure)	endovascular
					Control:	I: 17 (9%)	angiography or
		Exclusion criteria:			2/189 (1%)	C: 10 (5%)	intervention.
		1) inability to			All had no	P=0.17	
		obtain informed			laboratory		
		consent,			data	Requirement of	Infusion rates
		2) serum creatinine				hemodialysis	were decreased to
		≥8 mg/dl, eGFR ≤15				I: 4 (2%)	0.5 ml/kg/hour in
		ml/min/1.73 m ² at			<u>Incomplete</u>	C: 2 (1%)	patients with left
		rest,			<u>outcome</u>	P=0.69	ventricular
		end-stage renal			<u>data</u> :		ejection fraction
		disease on			As above	Rates of death,	≤45% in the 2
		hemodialysis,				myocardial	treatment arms.
		3) multiple				infarction, and	
		myeloma,				stroke did not	
		4) pulmonary				differ significantly	
		edema,				at 1 month and 6	
		5) uncontrolled				months after	
		hypertension				contrast exposure.	
		(systolic pressure					
		>160 mm Hg or					
		diastolic pressure					
		>100 mm Hg),					
		6) acute ST-					
		segment elevation					
		myocardial					
		infarction while					

undergoing primary precrutaneous intervention, 7 emergency coronary angloplasty or anglography, 8) use of contrast media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, manitol, fenoldopam, and NAC Nactorial at baseline: intervention: 193 control: 189 Brootat at baseline: intervention: 193 control: 189 Ser: i: 708 M c: 68 (67-72) Ser: i: 708 M c: 715 M c: 715 M c: 715 M	 		
intervention, 7) emergency coronary angiography, 8) use of contrast media within the previous 2 days, 9) prepancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC <u>Notal at baseline:</u> Intervention: 193 Control: 129 <u>Important</u> <u>propositic factors²: For example age median (IGR) <i>k</i>: 69 (63-72) <i>Sex:</i> <i>k</i>: 72% M</u>	undergoing primary		
7) emergency coronary angioplasty or angiography, 8) use of contrast media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 59 (63-73) C: 68 (67-72) Sex: 1: 708 M C: 718 M	percutaneous		
coronary angioplasty or angioplasty or angioplasty or anginglasty or anginglasty or </td <td>intervention,</td> <td></td> <td></td>	intervention,		
coronary angioplasty or angioplasty or angioplasty or anginplasty or anginplasty or </td <td>7) emergency</td> <td></td> <td></td>	7) emergency		
angiography, 8) use of contrast media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC NAC Important propositic factors ² : For example oge median (IQR) I: 59 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
angiography, 8) use fortrast media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopan, and NAC Note Note at baseline: intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C: 68 (67-72) Sex: 1: 70% M C: 71% M			
8) use of contrast media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C 58 (67-72) Sex: 1: 70% M C: 71% M			
media within the previous 2 days, 9) pregnancy, 10) allergy to contrast medium 111 medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC N total at baseling: intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) t: 69 (63-72) Sex: t: 70% M C: 71% M			
previous 2 days, 9) pregnancy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age medion (IQR) 1: 69 (63-73) Sex: 1: 70% M C: 71% M			
9) pregnançy, 10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC NAC Ntotal at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) i: 69 (63-73) C: 68 (67-72) Sex: i: 70% M c: 71% M Ci 71% M			
10) allergy to contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC NAC Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C: 68 (67-72) Sex: 1: 70% M C: 71% M			
contrast medium 11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC NAC Nac Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C: 68 (67-72)			
11) medications such as theophylline, dopamine, mannitol, fenoldopam, and NAC Nacc Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) i: 69 (63-73) c: 68 (67-72) Sex: I: 70% M C: 71% M			
such as theophylline, dopamine, mannitol, fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C: 68 (67-72) Sex: 1: 70% M C: 71% M			
theophylline, dopamine, mannitol, fenoldopam, and NAC NAC Ntotal at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
dopamine, mannitol, fenoldopam, and NAC NAC Ntotal at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M Sex: I: 70% M			
mannitol, fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
fenoldopam, and NAC N total at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
NAC Ntotal at baseline: Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) 1: 69 (63-73) C: 68 (67-72) Sex: 1: 70% M C: 71% M			
Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
Intervention: 193 Control: 189 Important prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M	N total at baseline:		
Important prognostic factors2:For example age median (IQR) 1: 69 (63-73) C: 68 (67-72)Sex: 1: 70% M C: 71% M			
prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M	Control: 189		
prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M			
prognostic factors ² : For example age median (IQR) I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M	Important		
For example age median (IQR) 1: 69 (63-73) C: 68 (67-72)	prognostic factors ² :		
I: 69 (63-73) C: 68 (67-72) Sex: I: 70% M C: 71% M	For example		
C: 68 (67-72) Sex: I: 70% M C: 71% M	age median (IQR)		
Sex: I: 70% M C: 71% M	I: 69 (63-73)		
1: 70% M C: 71% M	C: 68 (67-72)		
1: 70% M C: 71% M			
C: 71% M			
	I: 70% M		
eGFR:	C: 71% M		
eGFR:			
	eGFR:		

	I: 46 (34-53) C: 46 (37-53) Groups comparable at baseline? Yes					
Maioli, 2008 Type of study: randomized controlled trial Setting: elective patients, one center Country: Italy Source of funding: not reported	Inclusion criteria: 1) patients with pre-angiographic estimated creatinin clearance <60 ml/min 2) undergoing planned angiographic procedures Exclusion criteria: 1) creatinine clearance ≥ 60 ml/min n = 691 2) refusal to participate n = 18 3) administration of contrast medium within the previous 10 days n = 12 4) end stage renal disease n = 3 <u>N total at baseline</u> : Intervention: 250 Control: 252 <u>Important</u> prognostic factors ² : <i>For example</i> <i>age median (IQR)</i> :	Describe intervention (treatment/procedure/test): Sodium bicarbonate (154 mEq/l in dextrose and water) received 3 ml/kg for 1 h before contrast medium, followed by an infusion of 1 ml/kg/h for 6 h after the procedure. All patients received 600 mg oral NAC twice a day from the day before to the day after the procedure	Describe control (treatment/procedure/test): 1 ml/kg/h 0.9% sodium chloride for 12 h before and after the procedure	Length of follow-up: 5 days Loss-to- follow-up: Intervention: 4/252 (2%) 3 died 1 acute renal failure Control: 5/250 (2%) 4 died 1 acute renal failure Incomplete outcome data: As above	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an absolute increase of at least 0.5 mg/dl over baseline serum creatinine within 5 days after the administration of the contrast medium) I: 25 (10%) C: 29 (12%) P=0.60 CIN2 (=as a relative increase _25% over baseline serum creatinine within 5 days after contrast agent administration) I: 15% C: 21% P=0.13	Authors' conclusion: Hydration with sodium bicarbonate plus NAC before contrast medium exposure is not more effective than hydration with isotonic saline plus NAC for prophylaxis of CIN in patients with moderate-to- severe renal dysfunction.

		4					1
		I: 74 (67-79)				Death and acute	
		C: 74 (70-79)				renal failure, see	
						column "Follow-	
		Sex:				up" for numbers,	
		I: 57% M				no significant	
		C: 61% M				difference in	
						clinical events.	
		eGFR ± SD:					
		l: 43 ± 11					
		C: 42 ± 10					
		0					
		Groups comparable					
		at baseline? Yes					
Nieto-Rios,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors
2014	randomized	1) Inpatients in a	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	tertiary center,			5 days	(include 95%CI and	
		scheduled to	3 ml/kg of sodium bicarbonate	1 ml/ kg/hour of normal saline	0 4470	p-value if	Our investigation
	Setting:	undergo a	solution (150 mEq/L) one hour	solution, starting 12 hours before	Loss-to-	available):	showed that there
	elective	procedure with the	prior to procedure and then drip	and continuing 12 hours after	follow-up:	avanabicj.	were no
	patients,	nonionic	rate was decreased to 1 ml/	iohexol contrast	Intervention:	CIN	differences
	single center	radiographic	kg/hour until 6 hours post	ionexor contrast	7/107 (7%)	(= increase in	between normal
	single center	contrast agent	procedure		3 died	serum creatinine	saline solution
	Country:	iohexol.	procedure		1	on 25% or more	(extended
	Colombia	2) serum creatinine			⊥ withdrawed	within 2 days after	infusion) vs.
	COlombia	levels of at least 1.2			3 technical	administration of	bicarbonate
	Source of				difficulties		solution for
		mg/dL (106.1			difficulties	radiographic con-	
	funding: not	µmol/L) and/or			Control:	trast)	nephroprotection.
	reported	type 2 diabetics,				I: 12 (12%)	
		Fuelueien eriteri-			1/113 (1%)	C: 8 (7%)	
		Exclusion criteria:			1 died	RR: 1.68, 95% CI:	
		1) current clinical				0.72 – 3.94	
		diagnosis of			Incomplete	p>0.05	
		exacerbated			outcome		
		congestive heart			<u>data</u> :	Decompensated	
		failure, 2) ejection			As above	heart failure	
		fraction <35% by				I: 3 (3%)	
		previous				C: 7 (6%)	

echocardiography,	P=0.34	
3) signs of acute		
pulmonary edema		
within 48 hours		
before the		
procedure,		
4) systolic blood		
pressure <90 mmHg		
or requirement of		
vasopressors		
support,		
5) patients with		
exposure to		
contrast 30 days		
prior to the study,		
6) known allergy to		
contrast dye,		
7) chronic renal		
disease with dialysis		
therapy,		
8) criteria for		
dialytic urgency,		
9) pregnancy,		
10) requirement of		
an emergency		
procedure (e.g.,		
aortography for		
diagnosis of aortic		
aneurism),		
11) patients with		
serum potassium		
<3 mEq/L (because		
of the risk of		
hypokalemia		
induced by		
bicarbonate),		
12) uncompensated		

Shavit, Type of study: Type of study: Describe intervention Describe intervention Describe control Length of Outcome measures Authors'				1				,
shavit, Type of study: Type of study: Describe control Length of Outcome measures Shavit, Type of study: Describe intervention Describe control Length of Outcome measures								
Important In the previous 24 hours) 13) patient or physician refusal to participate. N total at baseline: Intervention: 107 Control: 113 Important progenostic factors ² : For example age ± 50; I: 61 ± 17 C: 60 ± 17 Sex: Sex: I: 57% M C: 58% M Baseline: SCr (mg/dL); I: 1.3 ± 0.3 C: 1.3 ± 0.3 </td <td></td> <td></td> <td>•</td> <td></td> <td></td> <td></td> <td></td> <td></td>			•					
sharit, Type of study: Type of study: Describe intervention Describe control Length of Outcome measures Authors'								
13) patient or physician refusal to participate. 13) patient or physician refusal to participate. 13) patient or physician refusal to participate. 1000000000000000000000000000000000000			in the previous 24					
Sex: :			hours)					
Shavit, Type of study: Inclusion criteria: Describe control Length of Outcome measures Authors'			13) patient or					
N total at baseline: Intervention: 107 Control: 113 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 61 ± 17 Important prognostic factors ² : For example age ± 5D: I: 57% M Important prognostic factors ² : For example age ± 5D: I: 57% M Important prognostic factors ² : For example age ± 5D: I: 13 ± 0.3 Important For example age ± 5D: I: 13 ± 0.3 Important For example age ± 5D: I: 13 ± 0.3 Important For example age ± 5D: Important For example For			physician refusal to					
Intervention: 107 Control: 113 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 57% M Important prognostic factors ² : l: 1.3 ± 0.3 C: 1.3 ± 0.3 Important prognostic factors ² : l: 1.3 ± 0.3 Important prognostic fa			participate.					
Intervention: 107 Control: 113 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : for example age ± 5D: l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : l: 57% M Important prognostic factors ² : l: 1.3 ± 0.3 C: 1.3 ± 0.3 Important prognostic factors ² : l: 1.3 ± 0.3 Important prognostic fa			N total at baseline:					
Sex: 1:57% M C:58% M Baseline SCr (mg/dL): 1:1.3 ± 0.3 C:1.3 ± 0.3 Groups comparable at baseline? Yes Shavit, Type of study: Inclusion criteria: Describe intervention Describe control Length of Outcome measures Authors'								
Important prognostic factors ² : For example age ± SD: I: 61 ± 17 C: 60 ± 17 Important prognostic factors ² : For example age ± SD: I: 51 ± 17 C: 60 ± 17 Important Sex: I: 57% M Sex: I: 57% M Sex: I: 57% M Important Sex: I: 57% M Important Save								
prognostic factors ² : For example age ± SD: I: 61 ± 17 C: 60 ± 17 For example age ± SD: I: 61 ± 17 C: 60 ± 17 Image: Constraint of the second s			Control. 115					
prognostic factors ² : For example age ± SD: I: 61 ± 17 C: 60 ± 17 For example age ± SD: I: 61 ± 17 C: 60 ± 17 Image: Constraint of the second s			Important					
For example age ± SD: 1: 61 ± 17 C: 60 ± 17 For example age ± SD: 1: 61 ± 17 C: 60 ± 17 Image: Constraint of the second								
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Image:								
C: 58% M Baseline sCr (mg/dL): I: 1.3 ± 0.3 C: 1.3 ± 0.3 Baseline sCr (mg/dL): I: 1.3 ± 0.3 Here is the second seco			Sex:					
Baseline sCr (mg/dL): I: 1.3 ± 0.3 C: 1.3 ± 0.3 Baseline sCr (mg/dL): I: 1.3 ± 0.3 Image: Comparable of the second s			I: 57% M					
Image: Market			C: 58% M					
Image: Market								
Image: 1.3 ± 0.3 Image: 1.3 ± 0.3 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>								
C: 1.3 ± 0.3 Groups comparable at baseline? Yes Length of Outcome measures Authors' Shavit, Type of study: Inclusion criteria: Describe intervention Describe control Length of Outcome measures Authors'								
Groups comparable at baseline? Yes Groups comparable at baseline? Yes Inclusion criteria: Describe intervention Describe control Length of Outcome measures Authors'								
at baseline? Yes at baseline? Yes Shavit, Type of study: Inclusion criteria: Describe intervention Describe control Length of Outcome measures			C: 1.3 ± 0.3					
at baseline? Yes at baseline? Yes Shavit, Type of study: Inclusion criteria: Describe intervention Describe control Length of Outcome measures Authors'			Groups comparable					
	Shavit,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2009 randomized 1) patients with (treatment/procedure/test): (treatment/procedure/test): <u>follow-up</u> : and effect size conclusion:	2009	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):		and effect size	conclusion:
controlled trial chronic kidney 2 days (include 95%Cl and		controlled trial	chronic kidney			2 days	(include 95%CI and	
disease (CKD) stage 154 mEq/L sodium bicarbonate in 12-hour infusion of 154 mEq/L p-value if Hydration with				154 mEq/L sodium bicarbonate in	12-hour infusion of 154 mEq/L		p-value if	Hydration with
Setting: III–IV undergoing 5% dextrose in water mixed by (0.9%) sodium chloride at a rate of Loss-to- available): sodium		Setting:				Loss-to-		
								bicarbonate is not

patier	ens,	catheterization	sodium bicarbonate to 846 mL of	catheterization and NAC 600 mg ×	Intervention:	CI-AKI	more effective
single	e-center		5% dextrose in water. The initial IV	2/d	0 (0%)	(=an increase of	than hydration
		Exclusion criteria:	bolus was 3 mL/kg for 1 hour	orally the day before and the day		25% or 0.3 mg/dL	with sodium
Count	ntry: Israel	1) plasma	before cardiac catheterization.	of the procedure	Control:	or more in plasma	chloride and oral
		creatinine levels	Following this bolus, patients		5/41 (12%)	creatinine within	NAC for
Sourc	ce of	more than	received the same fluid at a rate of		No	2 days of contrast	prophylaxis of CI-
fundir	ing: not	8 mg/dL or eGFR	1 mL/kg per hour during the		laboratory	administration)	AKI in patients
repor	rted	less than 15	contrast exposure and for 6 hours		evaluation at	I: 5/51 (10%)	with CKD stage III-
		mL/min, change in	after the procedure.		baseline or	C: 3/36 (8%)	IV undergoing
		plasma creatinine			after contrast	p>0.05	cardiac
		levels of ≥0.5 mg/dL	For patients weighing more than		exposure		catheterization.
		during the previous	110 kg, the initial fluid bolus and			CI-AKI2	
		24 hours,	drip were limited to those doses		Incomplete	(=an increase in	
		2) preexisting	administered to patients weighing		<u>outcome</u>	plasma creatinine	
		dialysis, multiple	110 kg.		<u>data</u> :	of 0.3 mg/dL or	
		myeloma,			As above	more from	
		3) pulmonary				baseline)	
		edema,				I: 17%	
		4) uncontrolled				C: 16%	
		hypertension				P>0.05	
		(systolic					
		>160 mmHg,				No patient	
		diastolic >100				developed more	
		mmHg),				than 50%	
		5) recent exposure				increment of	
		to radiographic				creatinine or	
		contrast, or other				required renal	
		nephrotoxic				replacement	
		medications (within				therapy during the	
		2 days of the				hospitalization.	
		study),					
		6) allergy to					
		radiocontrast,					
		7) pregnancy					
		N total at baseline:					
		Intervention: 51					

		Control: 36					
		Important prognostic factors ² : For example age ± SD: I: 72 ± 10 C: 71 ± 9					
		Sex: I: 84% M C: 70% M					
		eGFR (ml/min/1.73m ²) ± SD:					
		l: 43 ± 11 C: 40 ± 10					
		Groups comparable at baseline? Yes					
	1		nate versus saline: "other schedules"	for coronary angiography and/or percu	itaneous interver	ntion	1
Chong,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2015	randomized	1) adults >21 years	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled trial	of age;			48 hrs	(include 95%CI and	
		2) glomerular				p-value if	'The combination
	Setting:	filtration	I1: High-dose oral NAC with a	C1: Oral NAC and abbreviated	Loss-to-	available):	regimenwas not
	University	rate (GFR) of 15–60	sustained intravenous sodium	intravenous sodium bicarbonate	follow-up:		superior to
	Heart Centre	mL/min/1.73m2 –	chloride infusion (NAC group)	infusion (COM group)	I1: 28/185	CIN, which was	individual
	Country:	calculated by the			12: 29/182	defined as ≥25%	regimens in
	Singapore	abbreviated	I2: Intravenous sodium		C1: 25/181	increase of serum	preventing CIN in
		Modification	bicarbonate infusion (SOB			Cr concentration	patientswith
	Source of	of Diet in Renal	group)		Death:	or a ≥44 µmol/L	baseline renal
	funding: not	Disease (MDRD)			11: 0/185	(0.5mg/dL)	impairment. There
	reported	formula –			12: 1/182	increase in serum	was a trend
		3) scheduled to			C1: 2/181	Cr within 48 h of	suggesting that
		undergo elective				cardiac	the 12-hour

cardiac catheterisation with or without PCI	catheterisation or PCI	sustained sodium chloride prehydration
4) were able to	I1: 6.5%	regimen was more
receive pre-	12: 12.8%	protective than
hydration for 12 h.	C1: 10.6%	the 1-hour
	P=0.214	abbreviated SOB
Exclusion criteria:		regimen.'
1) end-stage renal		
failure with GFR of		
b15 mL/min/1.73		
m2,		
acute renal failure		
with a N44 μ mol/L		
increase in serum		
Cr levels in the		
previous 24 h;		
2) pre-existing		
dialysis;		
3) pulmonary		
oedema or		
moderate to severe		
congestive heart		
failure		
(New York Heart		
Association III–IV);		
4) inability to		
withstand the fluid		
load;		
5) presence		
of haemodynamic		
compromise,		
uncontrolled		
hypertension		
(untreated systolic		
blood pressure		
N160mmHg, or		

diastolic blood pressure N100mmHgl 6) emergency cardiac cardiaction 7) exposure to contrast in the previous two days; 8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) clipitali within 48 h of cardiac catheterisation and throughout the study duration; Important proposition factors ² - <i>for example</i> <i>gg z: 50:</i> <i>i, 69 zi 00</i>	r			1 1
N100mmHg) 6) emergency cardiac catheterisation 7) exposure to 7) exposure to contrast in the previous two days; 8) allergies to 7) exposure to contrast or NAC; 9) administration of sodium bicarbonate 7 or NAC within 48 h 6 of cardiac 7 catheterisation; 10) clinical conditions requiring 7 continuous fluid theraps such as severe sepsis; 11) Use of potentially renal- 10% clinical toxic drugs; 12 12 cipatin within 48 h of cardiac 11 catheterisation and throughout the study duration; important monostic factors ² ; for example age ± 50; if ± 51 ± 10 10				
6) emergency cardiac catheterisation 7) exposure to Contrast in the previous two days; 8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± 50: 1 69 ± 10				
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7) exposure to contrast in the previous two days; 8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10; dinical conditions requiring continuous fluid therapy such as severe spisis; 11) Use of potentially renal- toxic drugs; 11) Use of potentially renal- toxic drugs; 11 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; 11 11) Use of potentially renal- toxic drugs; 12 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; 11 11) Use of potentially renal- toxic drugs; 12 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; 11 11) Use of potentially renal- toxic drugs; 12 12) cisplatin within 48 h of cardiac catheterisation and throughout the study 12 13) Use of potentially renal- toxic drugs; 13 14) Use of potentially renal- toxic drugs; 14 12) cisplatin within 48 h of cardiac catheterisation and throughout the study 14 14) Use of potentially renal- toxic drugs; 14 15) J 15 16 16) J 16 16 17) J 16 16		cardiac		
contrast in the previous two days; 8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 100 100 citional conditions requiring conditions requiring conditions requiring 10 Use of potentially renal- toxic drugs; 12) cisplation within 48 h of cardiac catheterisation and throughout the study duration; more consitic factors ² ; For example conditions age ± \$10 conditions		catheterisation		
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8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± \$D: 1:69 ± 10		contrast in the		
8) allergies to contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± \$D: 1:69 ± 10		previous two days;		
contrast or NAC; 9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid theraps yuch as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important progenostic factors ² : For example age ± \$D; i: 69 ± 10				
9) administration of sodium bicarbonate or NAC within 48 h of cardiac catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important progeniatic factors ² : For example age ± 5D: i: 69 ± 10				
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of cardiac catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± 5D: 1: 69 ± 10				
catheterisation; 10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± 5D: i: 69 ± 10 i: 69 ± 10		or NAC within 48 h		
10) clinical conditions requiring continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± 5D: i: 69 ± 10		of cardiac		
$ \begin{array}{c} conditions requiring \\ continuous fluid \\ therapy such as \\ severe sepsis; \\ 11) Use of \\ potentially renal- \\ toxic drugs; \\ 12) cisplatin within \\ 48 h of cardiac \\ catheterisation and throughout the \\ study \\ duration; \\ \hline \hline$		catheterisation;		
$ \begin{array}{c} conditions requiring \\ continuous fluid \\ therapy such as \\ severe sepsis; \\ 11) Use of \\ potentially renal- \\ toxic drugs; \\ 12) cisplatin within \\ 48 h of cardiac \\ catheterisation and throughout the \\ study \\ duration; \\ \hline \hline$		10) clinical		
continuous fluid therapy such as severe sepsis; 11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± SD: l: 69 ± 10				
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severe sepsis;11) Use ofpotentially renal- toxic drugs;12) cisplatin within48 h of cardiac catheterisation and throughout the study duration;Important prognostic factors ² : For example $age \pm 5D$: $l: 69 \pm 10$		therapy such as		
11) Use of potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; $\frac{Important}{prognostic factors^2}$: For example $age \pm SD$: $l: 69 \pm 10$				
potentially renal- toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; $\frac{Important}{prognostic factors^{2}}:$ For example $age \pm SD:$ $I: 69 \pm 10$				
toxic drugs; 12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; $\frac{Important}{prognostic factors^{2}}:$ For example age \pm SD: 1: 69 \pm 10				
12) cisplatin within 48 h of cardiac catheterisation and throughout the study duration; $\frac{\text{Important}}{\text{prognostic factors}^2:}$ For example $age \pm SD:$ $i: 69 \pm 10$				
48 h of cardiac catheterisation and throughout the study duration; Important prognostic factors ² : For example age ± SD: i: 69 ± 10				
throughout the study duration; Important prognostic factors ² : For example age ± SD: l: 69 ± 10		48 h of cardiac		
study duration; Important prognostic factors ² : For example age ± SD: 1: 69 ± 10		catheterisation and		
duration; Important prognostic factors ² : For example age ± SD: 1: 69 ± 10		throughout the		
Important prognostic factors ² : For example age ± SD: l: 69 ± 10		study		
prognostic factors ² : For example age ± SD: 1: 69 ± 10		duration;		
prognostic factors ² : For example age ± SD: 1: 69 ± 10				
prognostic factors ² : For example age ± SD: 1: 69 ± 10		Important		
For example age ± SD: l: 69 ± 10		prognostic factors ² :		
age ± SD: I: 69 ± 10				
<i>I: 69 ± 10</i>				
		l2: 71 ± 10		

		C: 67 ± 10					
		0.07 ± 10					
		Sex:					
		I1: 72% M					
		12: 78% M					
		C: 78% M					
		0. 7070 111					
		Groups comparable					
		at baseline? Yes					
Motohiro,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2011	randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
2011	controlled trial	undergoing		(inclution) procedure, cest,	1 months	(include 95%CI and	conclusion
		coronary	0.9% sodium chloride for 12 hours	0.9% sodium chloride for 12 hours	2	p-value if	Sodium chloride
	Setting:	angiography or	before and after the procedure.	before and after the procedure.	Loss-to-	available):	plus sodium
	elective	intervention			follow-up:	aranasie,	bicarbonate is
	patient, 2	2) \geq 20 years old	Sodium bicarbonate solution was		Intervention:	CIN	more effective
	hospitals	3) had an estimated	prepared by adding 154 ml of		2/79 (2%)	(=25% increase or	than sodium
	noopitalo	glomerular	sodium bicarbonate 1,000 mEq/L		No	an absolute	chloride alone for
	Country: Japan	filtration rate	to		laboratory	increase of	prophylaxis of CIN
	ee and yr eap an	(eGFR) <60	846 ml of 5% dextrose in water. In		test results	0.5 mg/dl in	and can lead to
	Source of	ml/min/1.73 m ²	the sodium bicarbonate group the			serum creatinine	retention of
	funding: not	,,	sodium bicarbonate solution was		Control:	from baseline	better long-term
	reported	Exclusion criteria:	changed 3 hours before contrast		1/79 (1%)	value, which	renal function.
		1) serum creatinine	administration		Angialgia	appeared within 2	
		levels >4 mg/dl,			due to	days of the	
		2) changes in serum			sodium	produce)	
		creatinine levels of			bicarbonate	1: 2 (3%)	
		≥0.5 mg/dl during			infusion	C: 10 (13%)	
		the previous 24				P=0.02	
		hours,			Incomplete	relative risk 0.176,	
		3) pre-existing			outcome	95% confidence	
		dialysis,			data:	interval	
		4) pulmonary			As above	0.037 to 0.83	
		edema,					
		5) uncontrolled				No patient required	
		hypertension				Hemodialysis.	
		(treated systolic				,	

							, , , , , , , , , , , , , , , , , , , ,
		blood pressure					
		>160 mm Hg or					
		diastolic blood					
		pressure >100 mm					
		Hg),					
		6) emergency					
		catheterization,					
		7) exposure to					
		radiographic					
		contrast within					
		previous					
		2 days,					
		8) any allergy to					
		radiographic					
		contrast medium					
		<u>N total at baseline</u> :					
		Intervention: 77					
		Control: 78					
		Important 2					
		prognostic factors ² :					
		For example					
		age ± SD:					
		1: 74 ± 7					
		C: 71 ± 9					
		C					
		Sex:					
		1: 64% M					
		C: 76% M					
		Groups comparable					
		Groups comparable at baseline? Yes					
Tamura	Tupo of study:		Describe intervention	Describe control	Length of	Outcomo monoures	Authors'
Tamura,	Type of study:	Inclusion criteria:				Outcome measures and effect size	
2009	randomized	1) Patients who	(treatment/procedure/test):	(treatment/procedure/test):	<u>follow-up</u> :		conclusion
	controlled trial	were scheduled for	Standard bydration with codium	Standard by dration with codium	3 days	(include 95%CI and p-value if	In conclusion
		elective coronary	Standard hydration with sodium	Standard hydration with sodium		p-value li	In conclusion,

Setting:	arteriography or	chloride plus single-bolus	chloride alone	Loss-to-	available):	single-bolus
elective	percutaneous	intravenous administration of		follow-up:		intravenous
patients,	•	sodium bicarbonate (20 ml /20	(=intravenous administration with	All patients	CIN	administration of
hospitals	intervention	mEq; Meyron 84, Otsuka	isotonic saline (0.9%) at a rate of 1	completed	(=an increase ≥25%	sodium
neopicale	2) age >20 years	Pharmaceutical,	ml/kg/hour (0.5 ml/kg/hour for	the study	or ≥ 0.5 mg/dl in	bicarbonate in
Country:		Inc., Tokyo, Japan) 5 minutes	patients with left ventricular	the stady	serum Cr within the	addition to
country in	(Cr) level >1.1 to	before contrast exposure	ejection fraction <40%) for 12	Incomplete	first 3 days after	standard
Source of			hours before and 12 hours after an	outcome	the procedure	hydration can
funding: r	•		elective coronary procedure. For	data:	compared to	more effectively
reported	Exclusion criteria:		patients weighing >80 kg, infusion	All patients	baseline value)	prevent CIN than
. epoted	1) allergy to		rate was limited to 80 ml/hour (40	completed	l: 1.4%	standard
	contrast medium,		ml/hour for patients with left	the study	C: 12.5%	hydration alone in
	pregnancy,		ventricular ejection fraction 40%).		P=0.017	patients with mild
	2) history of					renal insufficiency
	dialysis,				Adverse clinical	undergoing an
	3) exposure to				events (acute	elective coronary
	contrast-medium				pulmonary edema,	procedure.
	within the				acute renal failure	
	preceding 48 hours				requiring dialysis,	
	of the study,				and death within 7	
	4) acute coronary				days of procedure)	
	syndrome within				1:0%	
	the preceding 1				C: 1.4%	
	month of the study,				p>0.05	
	5) severe symptoms					
	of heart failure					
	(New York Heart					
	Association					
	functional class IV),					
	6) left ventricular					
	ejection fraction					
	>25%,					
	7) severe chronic					
	respiratory disease,					
	8) single					
	functioning kidney,					
	9) administration of					

		N-acetylcysteine, theophylline, dopamine, or mannitol					
		<u>N total at baseline</u> : Intervention: 72 Control: 72					
		Important prognostic factors ² : For example age ± SD: I: 73 ± 8 C: 72 ± 10					
		Sex: I: 83% M					
		С: 92% М					
		Groups comparable at baseline? Yes					
Turedi, 2016	Type of study: randomized controlled trial	Inclusion criteria: 1) Undergoing contrastenhanced thoracic CT due to	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	<u>Length of</u> <u>follow-up</u> : 48-72 hrs	Outcome measures and effect size (include 95%Cl and p-value if	Authors' conclusion 'In conclusion,
	Setting: academic	suspected PE; 2) aged over	I1: 3 mL/kg intavenous NAC+NS solution (3 g NAC was made up to	C1: NS alone 1 hour before CTPA and 1 mL/kg intavenous per hour	Loss-to- follow-up:	available):	there were no statistically
	emergency	18 years;	1000 mL with NS),	for a minimum of 6 hour after	11: 7/85	CIN development	significant
	center	 with measure- able basal 		СТРА.	12:8/85	creatinine levels	differences observed
	Country:	creatinine levels	I2: NaHCO3 + NS solution (132 mEq NaHCO3 was made up to		C1: 11/87	and post-CTPA creatinine	among
	Turkey	pretomography	1000 mL with NS)		Death:	levels measured	prophylactic NAC,
		and;			11: 4/85	48–72 hours	NaHCO3, and NS
	Source of funding: not	4) measureable serum creatinine			I2: 2/85 C1: 6/87	following contrast exposure	in prevention of CIN following
	reported	levels 48– 72 hours				and an increase	contrast-enhanced

	I	 	0704 (
posttomography,		≥25% or 0.5 mg/dL	CTPA.'
and with one or			
more of the		11: 23.5%	
risk factors for CIN.		12: 21.2%	
The risk		C1: 26.4%	
factors were		P=0.719	
preexisting renal			
dysfunction (Cr 1.4			
mg/dL or a high or			
calculated			
glomerular			
filtration rate			
[GFR] < 60			
mL/min/1.73 m ²),			
diabetes mellitus,			
hypertension			
receiving			
treatment,			
hypotension			
(systolic blood			
pressure < 90 mm			
Hg), coronary artery			
disease, history of			
nephrotoxic drug			
use (nonsteroidal			
anti-inflammatory			
drugs, cisplatin,			
aminoglycoside,			
amphotericin B),			
liver disease,			
congestive heart			
failure (active or			
history thereof),			
age 75 or over, and			
anemia (hematocrit			
< 30%).			

	1	1	
Exclusion criteria:			
1) end-stage renal			
disease already in			
peritoneal dialysis;			
2) hemodialysis;			
3) pregnant			
women;			
4) subjects with a			
known allergy to			
NAC or NaHCO3;			
5) patients			
requiring NAC			
therapy or NaHCO3			
therapy			
for existing			
additional disease;			
6) exposed to			
contrast			
material for any			
reason in the			
previous 10 days or			
7) during the in-			
hospital follow-up			
period			
8) patients			
who refused to			
participate			
Important			
prognostic factors ² :			
For example			
age ± SD:			
1: 76 (72-80)			
12: 77 (71-80)			
C: 74 (73-76)			
Sex:			
		*	

Ueda, 2011	Type of study:	I1: 48% M I2: 51% M C: 53% M Groups comparable at baseline? Yes Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
	randomized controlled trial Setting: emergency patients, single center Country: Japan Source of funding: not reported	Inclusion criteria:1) patientsundergoing anemergent (within60 minutes ofadmission)diagnostic orinterventionalcoronaryprocedure, such ascoronaryprocedure, such ascoronaryangiography orpercutaneouscoronaryintervention2) >20 years old3) had renalinsufficiency,defined by a serumcreatinine(Cr) concentrationof >1.1 mg/dl orestimatedglomerual filtrationrate (eGFR) of <60	Intravenous bolus injection of 154 mEq/L of sodium bicarbonate at a dose of 0.5 ml/kg, as soon as possible after they were admitted, before the administration of the contrast medium Intravenous infusion of 154 mEq/L sodium bicarbonate at 1 ml/kg/hour during and for 6 hours after the coronary procedure	Intravenous bolus injection of 154 mEq/L of sodium chloride at a dose of 0.5 ml/kg, as soon as possible after they were admitted, before the administration of the contrast medium Intravenous infusion of 154 mEq/L sodium bicarbonate at 1 ml/kg/hour during and for 6 hours after the coronary procedure	Length of follow-up: 2 days Loss-to- follow-up: Intervention: 0 (0%) Control: 1/30 (3%) Circulatory failure Incomplete outcome data: As above	outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase by >25% or >0.5 mg/dl of the serum creatinine level within 2 days after the procedure) I: 1 (3%) C: 8 (28%) RR: 0.12, 95% Cl: 0.016 – 0.91 P=0.01 Congestive heart failure I: 5/30 (17%) C: 6/29 (21%) p>0.05 Death I: 2/30 (7%) C: 2/29 (7%) p>0.05 No patients	Authors conclusion In conclusion, rapid alkalization by bolus injection of sodium bicarbonate was effective for the prevention of CIN in patients with CKD undergoing emergent procedures.

[]		Г /	
	>0.5 mg/dl during		developed acute
	the 24 hours before		renal failure
	the procedure,		requiring
	2) pre-existing		hemodialysis.
	dialysis, exposure		
	to the contrast		
	media within 2 days		
	before the study,		
	3) allergy to the		
	contrast media,		
	pregnancy,		
	4) previous or		
	planned		
	administration of		
	mannitol,		
	fenoldopam, N-		
	acetylcysteine,		
	theophylline,		
	dopamine, or		
	nonstudy sodium		
	bicarbonate		
	N total at baseline:		
	Intervention: 30		
	Control: 29		
	Important_		
	prognostic factors ² :		
	For example		
	age ± SD:		
	l: 77 ± 9		
	<i>C</i> : 75 ± 10		
	Sex:		
	I: 79% M		
	C: 77% M		
	I I	I	

		sCr (mg/dL) ± SD:					
		I: 1.32 ± 0.46					
		C: 1.51 ± 0.59					
		$C. 1.51 \pm 0.59$					
		Groups comparable					
		at baseline? Yes					
			ium bicarbonate short schedule versus	saline long schedule for computed to	nography		
Kooiman,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2014	randomized	1) In- and	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled trial	outpatients			96 hours	(include 95%CI and	
		electively	250 mL intravenous 1.4% sodium	2000 mL of intravenous 0.9%		p-value if	Short hydration
	Setting:	, scheduled for CE-CT	bicarbonate 1 h prior to CE-CT	saline, 1000 mL prior to and 1000	Loss-to-	available):	, with sodium
	elective	regardless of the	without hydration post-CE-CT	mL post-CE-CT	follow-up:	,	bicarbonate prior
	patients,	indication	, ,		Intervention:	CI-AKI	to CE-CT was non-
	multi-center	2) least 18 years of			15/267(6%)	(=serum creatinine	inferior to peri-
	trial	age, had CKD (eGFR			2 treated	increase >25%/>44	procedural saline
		<60 mL/min/1.73			according to	µmol/L (0.5 mg/dL)	hydration with
	Country: the	m ² estimated by			protocol	1:8 (3%)	respect to renal
	Netherlands	the Modification of			5 CT without	C: 14 (5%)	safety and may
		Diet in Renal			iv contrast	P=0.23	result in
	Source of	Disease formula			6 CT		healthcare
	funding: non-	3) eligible for the			cancelled and	Recovery of kidney	savings.
	commercial	fluid challenge of			no hydration	function:	
		saline hydration				I: 75%	
					Control:	C: 69%	
		Exclusion criteria:			20/281 (7%)	P=0.81	
		1) pregnancy,			7 treated		
		previous contrast			according to	Acute heart failure	
		administration			protocol	due to volume	
		within the last 7			7 CT	expansion (based	
		days,			cancelled and	on the	
		documented			no hydration	treating physician's	
		allergy for			4 CT without	clinical judgement)	
		iodinated contrast			iv contrast	occurred in none of	
		media,			2 treated	the patients in the	
		 haemodynamic 			with sodium	sodium	
		instability (systolic			bicarbonate	bicarbonate group	

	-		1				
		blood				versus 6 of 281	
		pressure <100			Incomplete	patients in the	
		mmHg)			outcome	saline group (P =	
		5) previous			<u>data</u> :	0.03)	
		participation in the			As above		
		trial				None of the CI-AKI	
						patients developed	
		N total at baseline:				a need for dialysis.	
		Intervention: 267				,	
		Control: 281					
		Important					
		prognostic factors ² :					
		For example					
		age ± SD:					
		I: 72 ± 10					
		C: 73 ± 10					
		Sex:					
		I: 60% M					
		C: 61% M					
		Mean eGFR:					
		I: 50 ± 13					
		C: 51 ± 14					
		Groups comparable					
		at baseline? Yes					
	•	•	Controlled diuresis for coronary angi	ography and/or percutaneous interven	ition	•	
Barbanti,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2016	randomized	1) All patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion
	controlled trial	symptomatic severe			78 hrs	(include 95%CI and	
		aortic stenosis	RenalGuard therapy received	control group received		p-value if	ʻln summary,
	Setting:	undergoing TAVI	hydration with a normal saline	sodium normal saline solution at a	Loss-to-	available):	furosemide-
	university	were considered	solution; with an initial bolus	rate of 1 ml/kg/h	follow-up:		induced diuresis
	hospital	eligible	(priming) of 250 ml was infused	12 h before TAVR, during contrast	No loss to	AKI	with matched
		Exclusion criteria:	over 30 min (preprocedural. Urine	exposure, and for 6 h after the	follow-up	(defined: absolute	isotonic

Country: Italy	1) chronic end-	flow was monitored and	procedure.	reduction in kidney	intravenous
	stage renal failure	maintained at the target value		function (<72 h)	hydration using
Source of	on dialysis;	throughout the procedure		and defined as: 1)	the RenalGuard
funding: not	2) episode of acute	and during the following 4 h.		stage 1: increase in	system
reported	congestive heart	phase).		serum creatinine to	is an effective
	failure with left			150% to 200% (1.5	therapeutic tool to
	ventricular ejection			to 2.0x increase	reduce the
	fraction <30% in the			compared with	occurrence of AKI
	past 30 days			baseline) or	in patients
	before			increase of >0.3	undergoing TAVR.'
	randomization;			mg/dl (≥26.4	
	3) contraindica-			mmol/l); 2) stage 2:	
	tions to placement			increase in serum	
	of a Foley catheter;			creatinine to 200%	
	4) urgent TAVI			to 300% (2.0 to	
	5) unavailability of			3.0x increase	
	the RenalGuard			compared with	
	system.			baseline); and 3)	
				stage 3: increase in	
	<u>Important</u>			serum creatinine to	
	prognostic factors ² :			≥300% (>3_	
	For example			increase compared	
	age ± SD:			with baseline) or	
	I: 82 (78-83)			serum creatinine of	
	C: 81 (78-84)			≥4.0 mg/dl	
				(≥354 mmol/l) with	
	Sex:			an acute increase	
	I: 61% F			of at least 0.5	
	C: 59% F			mg/dl (44 mmol/l).)	
	Serum creatine ± SD			l: 4 (5.4%)	
	I: 1.0 (0.85-1.15)			C: 13 (25.2%)	
	C: 0.97 (0.83-1.16)			RR: 0.21, 95% CI:	
	-/			0.06 - 0.71	
	Groups comparable			P=0.014	
	at baseline? Yes				
				Cardiovascular	

						death I: 0/56(0%) C: 1/56 (1.8%) P=0.306 Death I: 1/56 (1.8%) C: 2/56 (3.6%) P=0.537	
Brar, 2014	Type of study: randomized controlled trial Setting: elective patients, 1 center Country: United states of America Source of funding: not reported	Inclusion criteria: 1) patients referred to the cardiac catheterisation laboratory 2) an estimated glomerular fi Itration rate (GFR) of 60 mL/min per 1 • 73 m ² or lower; 3) age 18 years or older; 4) at least one of the following: diabetes mellitus, history of congestive heart failure, hypertension (blood pressure >140/90 mm Hg or treatment with antihypertensive medication), or age older than 75 years.	Describe intervention (treatment/procedure/test): 0.9% sodium chloride bolus infusion at 3 mL/kg for 1 h The fl uid rate was adjusted according to the left ventricular end-diastolic pressure as follows: 5 mL/kg/h for left ventricular end- diastolic pressure lower than 13 mmHg, 3 mL/kg/h for pressure of 13–18 mmHg, and 1.5 mL/kg/h for pressure higher than 18 mmHg. The fl uid rate was set at the start of the procedure (before contrast exposure), continued for the duration of the procedure, and for 4 h post- procedure.	Describe control (treatment/procedure/test): 0.9% sodium chloride bolus infusion at 3 mL/kg for 1 h 5 mL/kg per h. The fl uid rate was set at the start of the procedure (before contrast exposure), continued for the duration of the procedure, and for 4 h post-procedure.	Length of follow-up: 2-8 weeks for laboratory parameters 6 months for clinical events Loss-to- follow-up: Intervention: 0 (0%) Control: 0 (0%) Incomplete outcome data: Intervention: 18/196 (9%) 12 had 1 sCr value 6 had no sCr value	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=a greater than 25% or 0.5 mg/dL increase in the serum creatinine concentration) I: 12/178 (7%) C: 28/172 (16%) RR: 0.41, 95% Cl: 0.22 – 0.79, p=0.005 6-months mortality I: 0.5% C: 4% P=0.037 No significant difference in other adverse clinical	Authors' conclusion: Left ventricular end-diastolic pressure-guided fl uid administration seems to be safe and eff ective in preventing contrast-induced acute kidney injury in patients undergoing cardiac catheterisation.
		Exclusion criteria: 1) inability to			Control:	events at 30 days or 6 months	

	-			
obtain consent		28/200 (14%)		
from participants,		24 had 1 sCr	In total, six patients	
2) emergency		value	(1 • 5%)—three in	
cardiac		4 had no sCr	each group—	
catheterisation (eg,		value	terminated the	
primary			intravenous fl uids	
percutaneous			early, the reason	
coronary			for which was	
intervention for ST-			shortness of breath	
segment elevation			in all six patients.	
myocardial				
infarction),				
3) renal				
replacement				
therapy,				
4) exposure to				
radiographic				
contrast media				
within the previous				
2 days,				
5) allergy to				
radiographic				
contrast media,				
6) acute				
decompensated				
heart failure,				
7) severe valvular				
heart disease,				
8) mechanical				
aortic prosthesis,				
9) left ventricular				
thrombus,				
10) history of				
kidney or heart				
transplantation,				
11) change in				
estimated GFR of				

		7.5% or more per					
		day or a cumulative					
		change of 15% or					
		-					
		more during the pre					
		ceding 2 or more					
		days.					
		N total at baseline:					
		Intervention: 196					
		Control: 200					
		Important					
		prognostic factors ² :					
		For example					
		age ± SD:					
		l: 71 ± 9					
		C: 72 ± 8					
		Sex:					
		I: 64% M					
		C: 59% M					
		C. 3570 W					
		eGFR ± SD					
		l: 48 ± 9					
		C: 48 ± 9					
		Groups comparable					
		at baseline?					
Briguori,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2011	randomized	1) patients with	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	chronic kidney			1 week	(include 95%CI and	
		disease scheduled	hydration with normal saline plus	154 mEq/L sodium bicarbonate in		p-value if	RenalGuard
	Setting:	for coronary and/or	NAC controlled by the RenalGuard	dextrose and H2O.	Loss-to-	available):	therapy is
	elective	peripheral	system	The initial intravenous bolus was 3	follow-up:		superior to
	patients,	angiography and/or		mL/kg per hour for at least 1 hour	0 (0%) in	CI-AKI	sodium
	multicenter	angioplasty with an	NAC was administered only iv	before contrast injection. Then, all	both groups	(=an increase in sCr	bicarbonate and
		estimated	(1500 mg in 1L saline) during the 3	patients received the same fluid at		concentration ≥0.3	N-acetylcysteine

Country: Italy	glomerular	phases (preprocedural,	a rate of 1 mL/kg per hour during	Incomplete	mg/dL above the	in preventing
	filtration rate	intraprocedural, and	contrast exposure and for 6 hours	<u>outcome</u>	baseline value at 48	contrast-induced
Source of	(eGFR) ≤30mL	postprocedural) of the RenalGuard	after the procedure.	<u>data</u> :	hours after	acute kidney
funding: not	/min/ 1.73 m ²	therapy.		Intervention:	administration of	injury in high-risk
reported	and/or a risk score		NAC orally at a dose of 1200 mg	0 (0%)	Contrast or the	patients.
	≥11)		twice daily the day before and the		need fordialysis)	
			day of administration of the	Control:	I: 16/146 (11%)	
	Exclusion criteria:		contrast agent (for a total of 2	3/147 (2%)	C: 30/146 (21%)	The risk score for
	1) acute myocardial		days)	2	Odds ratio: 0.47,	predicting CI-AKI
	infarction;		additional NAC dose (1200 mg	discontinued	95% CI 0.24 – 0.92	was calculated
	2) acute pulmonary		diluted in 100 mL normal	treatment	P<0.05	according to the
	edema;		saline) was administered	1 did not		following
	3) cardiogenic		intravenously during the	receive		algorithm:
	shock;		procedure.	allocated		hypotension
	4) dialysis;		The total NAC dose was 6 g.	treatment		(integer score 5),
	5) multiple					intra-aortic
	myeloma;					balloon pump
	6) administration of					support (integer
	sodium					score 5),
	bicarbonate,					congestive heart
	theophilline,					failure (integer
	dopamine,					score 4), age >75
	mannitol,					years (integer
	and/or					score 4), diabetes
	fenoldopam;					mellitus (integer
	7) recent (<48					score 3), eGFR _60
	hours)					mL/min/1.73 m ²
	administration of					(integer score 2 to
	iodinated contrast					6), preexisting
	medium					anemia(integer
	8) enrollement in					score 3), and CM
	another study					volume (integer
						score 1 for each
	N total at baseline:					100 cm ³).
	Intervention: 146					The global scores
	Control: 146					≥5, 6 to 10, 11 to
						16, and _16

		Important prognostic factors ² : For example age ± SD: I: 76 ± 8					predict a CI-AKI risk of 7.5%, 14%, 26.1%, and 57.3%, respectively.
		C: 75 ± 9 Sex: I: 61% M C: 71% M					
		eGFR ± SD: 1: 32 ± 7 C: 32 ± 9					
		Groups comparable at baseline? Yes					
Marenzi,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome measures	Authors'
2012	randomised	1) age ≥18 years	(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	and effect size	conclusion:
	controlled trial	and ≤85 years, and			72 hours	(include 95%CI and	
		elective or urgent		continuous intravenous infusion of		p-value if	In patients with
	Setting:	(within 24 h from	Approximately 90 min before the	isotonic saline at a rate of 1	Loss-to-	available):	CKD undergoing
	elective and	hospital admission	coronary procedure, Furosemide	ml/kg/h (0.5ml/kg/h in case of left	follow-up:		coronary
	emergency	because of non–ST-	with matched hydration treatment	ventricular ejection fraction ≤40%)	Intervention:	CIN	procedures,
	patients	segment elevation	was started with an initial	for at least 12 h before and 12 h	2/89 (2%)	(=a ≥25% or ≥0.5	furosemide-
		[acute] myocardial	intravenous bolus (250 ml) of	after the procedure.	Failed to	mg/dl rise in serum	induced high urine
	Country: Italy	infarction	normal saline solution over 30 min.		insert foley	creatinine over	output with
		[NSTEMI]) coronary	Furosemide was then administered		catheter	baseline during the	matched
	Source of	angiography and,	as a single intravenous bolus of 0.5			first 72 h post-	hydration
	funding: not	when indicated,	mg/kg (up to a maximum of 50		Control:	procedure)	significantly
	reported	percutaneous	mg).		2/85 (2%)	I: 4 (5%)	reduces the risk of
		coronary	Urine output was calculated		Withdrawal	C: 15 (18%)	CIN and may be
		intervention (PCI).	continuously by the system, and		of treatment	P=0.005	associated with
			when a urine output rate >300		due to		improved in-
		Exclusion criteria:	ml/h was achieved, patients were		pulmonary	Cumulative in-	hospital outcome.
		1) primary or	brought to the catheterization		edema	hospital	
		rescue PCI and	laboratory and underwent			complications	

		1		
angiography	coronary angiography. Matched	Incomplete	I: 8%	
procedures	hydration was continued	<u>outcome</u>	C: 18%	
requiring a direct	throughout the catheterization	data:	P=0.052	
renal injection of	procedure and for 4 h after the last	As described		
contrast,	contrast dose. At this time, therapy	above)		
2) cardiogenic	was discontinued.			
shock, overt	Additional doses of furosemide (up			
congestive heart	to a maximal cumulative dose of			
failure,	2.0 mg/kg) were given in cases			
3) acute respiratory	where the urine output was below			
insufficiency,	300 ml/h during treatment. The			
4) recent acute	Foley catheter was removed 24 h			
kidney injury,	after the procedure.			
5) chronic				
peritoneal				
or hemodialysis				
treatment,				
6) known				
furosemide				
hypersensitivity,				
7) receipt of				
intravenous				
contrast within 10				
days before the				
procedure or				
another planned				
contrast-enhanced				
procedure in the				
following 72 h,				
8) contraindications				
to placement of a				
Foley catheter in				
the bladder.				
<u>N total at baseline</u> :				
Intervention: 87				
Control: 83				

Qian, 2016	Type of study: randomised controlled trial Setting: elective patients, multiple centers Country: Japan Source of funding: not reported	Important prognostic factors ² :For example $age \pm SD$: $l: 73 \pm 7$ $C: 74 \pm 8$ Sex: $l: 78\% M$ $C: 78\% M$ eGFR $\pm SD$: $l: 1.8 \pm 0.6$ $C: 1.7 \pm 0.5$ Groups comparable at baseline? YesInclusion criteria: 1) patients with CKD and chronic heart failure undergoing coronary proceduresExclusion criteria: $-$ N total at baseline: Intervention: 132 Control: 132Groups comparable at baseline? Yes	Describe intervention (treatment/procedure/test): Central-venous pressure guided hydration group	Describe control (treatment/procedure/test): Standard hydration group	Length of follow-up: 48 hours Loss-to- follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=an increase by >25% or >0.5 mg/dl of the serum creatinine level within 2 days after the procedure) I: 16% C: 30% P=0.006 Acute heart failure: I: 3.8%	Authors' conclusion: Controlled vnous pressure guided fluid administration can safely and effectively reduce the risk of CIN in patients with CKD and chronic heart failure.
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						C: 3.0% P=0.50	
Usmiani, 2015	Type of study: randomized controlled trial	<u>Inclusion criteria</u> : 1) patients with chronic kidney	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	<u>Length of</u> <u>follow-up</u> : 2 days	Outcome measures and effect size (include 95%CI and	Authors' conclusion:
	Setting: elective patients	disease (CKD) undergoing coronary procedures	iv 250 mL isotonic saline bolus, followed by a 0.5 mg/kg furosemide i.v. bolus to forced diuresis. A dedicated device automatically matched the isotonic	Standard saline and bicarbonate hydration	<u>Loss-to-</u> <u>follow-up</u> : Not reported	p-value if available): CI-AKI (=an increase by	In patients with CKD undergoing coronary procedures, furosemide-
	Country: Brazil	Exclusion criteria: -	saline i.v. infusion rate to the urinary output for 1h before, during and 4h after the procedure.		Incomplete outcome data:	>25% or >0.5 mg/dl of the serum creatinine level	induced high urine output with matched
	funding: not reported	<u>N total at baseline</u> : Intervention: 65 Control: 68			Not reported	within 2 days after the procedure) I: 7% C: 25% P=0.01	hydration significantly reduces the risk of CIN and may be associated with
		Groups comparable at baseline? Yes				Major adverse cardiovascular events I: 7% C: 32% P<0.01	improved in- hospital outcome.
Usmiani, 2016	Type of study: randomized controlled trial	Inclusion criteria: 1) Elgibile for voth procedures 2) eGFR of less than 60 mL/	Describe intervention (treatment/procedure/test): Matched hydration was to be	Describe control (treatment/procedure/test): BS-NAC intravenous hydration	<u>Length of</u> <u>follow-up</u> : 7 days	Outcome measures and effect size (include 95%Cl and p-value if	Authors' conclusion 'Matched
	Setting: university	min/1.73m2	performed with the Renal- Guard System.	(isotonic saline/ N-acetylcysteine/vitamin C)	<u>Loss-to-</u> <u>follow-up</u> :	available):	hydration was more effective
	hospital	Exclusion criteria: <u>1)</u> primary PCI	250 mL i.v. isotonic saline	1000 mL isotonic saline i.v.	9 loss to follow-up	AKI (CIAKI after	than BS-NAC in CIAKI
	Country: Italy Source of	(emergency procedure); 2) cardiogenic	bolus is given in 30 min, followed by 0.5 mg/kg i.v. furosemide to forced diuresis. Isotonic saline i.v.	administration 12 h before procedure (rate-adjusted according to LVEF 20–40mL/h if	I: 8/67 C: 1/66	coronary angiography/PCI as defined by an	prevention.'
	funding: not	 cardiogenic shock; 	infusion proceeds automatically,	LVEF<30%, 80–120 mL/h if LVEF		increase of sCr +0.3	

reported	3) acute heart	rate-matched with diuresis	30–50%, 200 mL/h if LVEF >50%).	mg/dL in 48 h or	
reported	failure;	rate-matched with didresis	50-50%, 200 mL/m LVEF >50%).	+50% in 7 days)	
	4) endstage		Plus 3 mL/kg/h 1.4% SB solution	+30% iii 7 uaysj	
	renal disease on		i.v. infusion for 1 h before	I: 4 (6%)	
	haemodialysis;		Plus: 5000mg p.o. Vitamin C	C: 16 (24%) P=0.01	
	5) urinary tract		Plus: 1200mg p.o. N-acetylcysteine	P=0.01	
	infections			Conditioners and an	
	within the last 3			Cardiovascular	
	months;			death	
	6) benign prostatic			I: 1/59(1.7%)	
	hyperplasia			C: 7/65 (10.8%)	
	and;				
	7) previously known				
	difficulties in				
	urinary				
	catheterization.				
	Important 2				
	prognostic factors ² :				
	For example				
	age ± SD:				
	l1: 76 ± 9				
	C: 75 ± 8				
	Sex:				
	l1: 22% F				
	C: 29% F				
	Serum creatine ± SD				
	l1: 1.54 ±0.43				
	C: 1.42 ±0.41				
	Groups comparable				
	at baseline? Yes				

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

CAG: Cardiac angiography; CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; CKD: chronic kidney disease; CT: computed tomography; CTPA: computed tomography – pulmonary angiography; ia: intra-arterial; IQR: intra quartile range; iv: intra-venous; NAC: N-acetylcysteine; PCI: percutaneous coronary intervention; sCr: serum creatinine

Search description

Systematic r	eviews
Database	Search terms
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.
(OVID) 2000-	(108416) 2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post adj1
heden Engels,	hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2
Nederlands	catheterization*)).ti,ab. (262412) 3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab. (525125)
	4 1 and 2 and 3 (911) 5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (8859) 6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2 catheterization*)).ti,ab. (262412) 7 5 and 6 (644)
	8 4 or 7 (1049) 9 limit 8 to (yr="2000 -Current" and (dutch or english)) (775) 10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (236842) 11 9 and 10 (69) – 66 uniek
	12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iii or clinical trial, phase iii or clinical trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1459903) 13 9 and 12 (333) 14 13 not 11 (278)
Embase (Elsevier)	'contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR
	(sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp)
	AND ('kidney disease'/exp OR 'kidney function'/exp OR ((kidney or renal) NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)
	OR ('contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR cin:ab,ti OR ciaki:ab,ti AND (induct* ich ti OD nephrodest* ich ti OD nephrodest* ich ti OD
	AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp))
1	inverteen / exp//

Total 177

'hydration'/exp)) AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py

AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomized controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it (484)

Cochrane (Wiley)	AND 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT (animal* NOT human*)), (137) - 82 uniek ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR cin:ab,ti OR ciaki:ab,ti AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization)) 15 CDR, 45 DARE	
	15 CDR, 45 DARE 11 CR's niet relevant (CIN-HPV) >4 uniek, DARE 25 uniek, 2 niet relevant	

RCTs		
Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	572
(OVID)	(110323)	RCTS
	2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
Engels,	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	6 SRs
Nederlands	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	new
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium	(177 SRs
2000-juni	adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	in earlier
2015	catheterization*)).ti,ab. (263883)	search
	3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*))	strategy)
	or nephropath* or (renal adj2 (insufficienc* or function* or disease* or	
	failure*))).ti,ab. (527891)	
	4 1 and 2 and 3 (918)	
	5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity))	
	or cin or ciaki).ti,ab. (8912)	
	6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	
	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid*)) or (sodium	
	adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	
	catheterization*)).ti,ab. or Water/ or water.ti,ab. or D5w.ti,ab. or Isotonic	
	Solutions/ or Hypotonic Solutions/ or (ringer* adj3 (lactate or solution*)).ti,ab. or	
	((hypotonic or isotonic) adj3 solution*).ti,ab. or Hydroxyethyl Starch Derivatives/	
	or (Hydroxyethy* adj3 starch*).ti,ab. (818303)	
	7 5 and 6 (733)	
	8 4 or 7 (1140)	
	9 limit 8 to (yr="2000 -Current" and (dutch or english)) (818)	
	10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or	
	((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw.	
	or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or	
	embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or	
	cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not	
	(Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (240088)	
	11 9 and 10 (72)	
	12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/	
	or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind	
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii	
	or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or	
	randomized controlled trial or multicenter study or clinical trial).pt. or	
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj	
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not	
	humans/) (1471469)	
	13 9 and 12 (341)	
	14 13 not 11 (283) – 265 uniek	
	17 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or	
	Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or	
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or	
	(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw.	
	or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically	

	controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2160769) 22 21 not 19 (134) – vanaf 2007: 105 – 103 uniek –in afzonderlijk document	
Embase (Elsevier)	'contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti	
	AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid*)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR water:ab,ti OR d5w:ab,ti OR (ringer* NEAR/3 (lactate OR solution*)):ab,ti OR ((hypotonic OR isotonic) NEAR/3 solution*):ab,ti OR (hydroxyethy* NEAR/3 starch*):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp OR 'hetastarch derivative'/exp OR 'fluid balance'/exp)	
	AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)	
	OR ('contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR cin:ab,ti OR ciaki:ab,ti	
	AND (hydrat*:ab,ti OR prehydrat*:ab,ti OR posthydrat*:ab,ti OR rehydrat*:ab,ti OR 'volume expansion':ab,ti OR (pre NEAR/1 hydrat*):ab,ti OR (post NEAR/1 hydrat*):ab,ti OR ((oral OR iv OR intravenous) NEAR/1 (hydrat* OR fluid*)):ab,ti OR (sodium NEAR/2 (chloride* OR bicarbonate)):ab,ti OR nacl:ab,ti OR ((heart OR cardiac) NEAR/2 catheterization):ab,ti OR water:ab,ti OR d5w:ab,ti OR (ringer* NEAR/3 (lactate OR solution*)):ab,ti OR ((hypotonic OR isotonic) NEAR/3 solution*):ab,ti OR (hydroxyethy* NEAR/3 starch*):ab,ti OR 'sodium chloride'/exp OR 'heart catheterization'/exp OR 'bicarbonate'/exp OR 'oral rehydration solution'/exp OR 'hydration'/exp OR 'hetastarch derivative'/exp OR 'fluid balance'/exp))	
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py	
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	
	NOT 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT (animal* NOT human*)) (517) – 307 uniek	

Observational studies

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	103
(OVID)	(110323)	obs.
	2 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
Engels,	Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	
Nederlands	posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	
	adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid)) or (sodium adj2	
2007-juni	(chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	
2015	catheterization*)).ti,ab. (263883)	
	3 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*))	

or nephropath* or (renal adj2 (insufficienc* or function* or disease* or	
failure*))).ti,ab. (527891)	
4 1 and 2 and 3 (918)	
5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity))	
or cin or ciaki).ti,ab. (8912)	
6 Sodium Chloride/ or exp Cardiac Catheterization/ or exp Bicarbonates/ or	
Rehydration Solutions/ or exp Fluid Therapy/ or (hydrat* or prehydrat* or	
posthydrat* or rehydrat* or 'volume expansion' or (pre adj1 hydrat*) or (post	
adj1 hydrat*) or ((oral or iv or intravenous) adj1 (hydrat* or fluid*)) or (sodium	
adj2 (chloride* or bicarbonate*)) or nacl or ((heart or cardiac) adj2	
catheterization*)).ti,ab. or Water/ or water.ti,ab. or D5w.ti,ab. or Isotonic	
Solutions/ or Hypotonic Solutions/ or (ringer* adj3 (lactate or solution*)).ti,ab. or	
((hypotonic or isotonic) adj3 solution*).ti,ab. or Hydroxyethyl Starch Derivatives/	
or (Hydroxyethy* adj3 starch*).ti,ab. (818303)	
7 5 and 6 (733)	
8 4 or 7 (1140) 9 limit 8 to (yr="2000 -Current" and (dutch or english)) (818)	
10 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or	
((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw.	
or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or	
embase.ab. or medline.ab. or (psychit or psyclit).ab. or (cinahl or cinhal).ab. or	
cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not	
(Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (240088)	
11 9 and 10 (72)	
12 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/	
or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind	
Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii	
or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or	
randomized controlled trial or multicenter study or clinical trial).pt. or	
random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj	
(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not	
humans/) (1471469)	
13 9 and 12 (341)	
14 13 not 11 (283) – 265 uniek	
17 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or	
Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or	
studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or	
(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw.	
or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically	
controlled study/ or interrupted time series analysis/ [Onder exp cohort studies	
vallen ook longitudinale, prospectieve en retrospectieve studies] (2160769)	
22 21 not 19 (134) – vanaf 2007: 105 – 103 uniek –in afzonderlijk document	

Evidence tables

Table: Exclusion after i	revision of full text
Author and year	Reason for exclusion
Aggarwal, 2014	Article not found
Atallah, 2004	Published before the SR of Liu, 2015
Ball, 2014	Review, not systematic
Barbieri, 2014	Did not include subgroup analyses with patients with renal dysfunction
Bidram, 2015	Patients with eGFR<60 excluded
•	
Bouzas-Mosquera, 2009	Published before the search date of SR of Liu, 2015
Cheungpasitporn, 2015	Did not include subgroup analyses with patients with renal dysfunction
Gandhi, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the literature analysis
Giacoppo, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the literature analysis
Han, 2014	Included in the review of Liu, 2015
Hoshi, 2014	Renal function not compromised, observational study
Jo, 2015	Article not available
Jo, 2008	Included in the review of Liu, 2015
Kandula, 2010	Published before the SR of Liu, 2015
Kaya, 2013	Published before the SR of Liu, 2015
Kenaan, 2014	Renal function not compromised, observation study
Lee, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Leoncini, 2014	Outcomes were the cardioprotective effects
Leoncini, 2014	Included in the review of Liu, 2015
Li, 2012	Published before the SR of Liu, 2015
Liu, 2014	Patients with eGFR of 30-90 mL/min/1.73m ² included, compared rosuvastatin with
210, 2014	atorvastatin
Mao, 2014	Did not include subgroup analyses with patients with renal dysfunction
Marenzi, 2015	Did not include subgroup analyses with patients with renal dysfunction
Munoz, 2011	Published before the SR of Liu, 2015
Ozhan, 2010	Published before the SR of Liu, 2015
Pappy, 2011	More recent SR available
Patti, 2014	Letter to the editor, substantial subgroup of patients has no renal dysfunction
Patti, 2008	Published before the SR of Liu, 2015
Patti, 2011	Included in the review of Liu, 2015
Peruzzi, 2014	No separate analysis for patients with renal dysfunction
Qiao, 2015	Patients with eGFR of 30-89 mL/min/1.73m ² included
Quintavalle, 2012	Included in the review of Liu, 2015
Sanadgol, 2012	Published before the SR of Liu, 2015
Sanei, 2014	Patients with normal renal function included
Shehata, 2015	Patients with eGFR of 30-90 mL/min/1.73m ² included
Singh, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the literature analysis
Takagi, 2011	More recent SR available
Toso, 2014	Used the data of Leoncini, 2013
Toso, 2010	Included in the review of Liu, 2015
Ukaigwe, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the literature analysis
Wu, 2015	Article not found
Xie, 2014	Overlapping with the systematic review of Liu, 2015, that was already included in the
	literature analysis
Xinwei, 2009	Published before the SR of Liu, 2015
Yoshida, 2009	Published before the SR of Liu, 2015
Yun, 2014	Observational study

Zhang, 2011	More recent SR available
Zhao, 2008	Published before the SR of Liu, 2015
Zhou, 2011	More recent SR available

Table: Exclusion after revision of full text (update 2017)

Author and year	Reason for exclusion
Ali-Hassan-Sayegh, 2016	Does not meet selection criteria, references were checked
Chalikias, 2016	Does not meet selection criteria, references were checked
Fan, 2016	No studies included after original search
Gadapa, 2016	Full text not available
Giacoppo, 2015	Full text not available
Jo, 2015	Does not meet selection criteria
Li, 2016	Does not meet selection criteria
Navarese, 2017	Does not meet selection criteria
Rabbat, 2015	Abstract
Subramaniam, 2016	Does not meet selection criteria, references were checked
Thompson, 2016	No studies included after original search
Vanmassenhove, 2016	No studies included after original search
Wang, 2016	No studies included after original search
Zografos, 2016	Full text not available
Zografos, 2016	No studies included after original search
Zografos, 2016	No studies included after original search
Fu, 2015	Full text not available
Gaskina, 2016	Abstract
Gaskina, 2016	Abstract
Maskon, 2016	Abstract
Park, 2016	Full text not available
Kohsravi, 2016	Does not meet selection criteria
Li, 2016	Does not meet selection criteria

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097;

doi:10.1371/journal.pmed1000097)

Study	Appropriate	Comprehensive	Description of	Description of	Appropriate adjustment for	Assessment of	Enough	Potential risk	Potential
	and clearly	and systematic	included and	relevant	potential confounders in	scientific	similarities	of publication	conflicts of
	focused	literature	excluded	characteristics	observational studies? ⁵	quality of	between	bias taken into	interest
	question? ¹	search? ²	studies? ³	of included		included	studies to	account? ⁸	reported? ⁹
				studies? ⁴		studies? ⁶	make		
							combining		
							them		
First							reasonable? ⁷		Yes/no/unclear
author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	
year Liu, 2015	Yes/no/unclear yes	Yes/no/unclear Yes	Yes/no/unclear No (excluded	Yes/no/unclear yes	Yes/no/unclear/notapplicable NA	Yes/no/unclear Yes	Yes/no/unclear Unclear		Yes (none of
-									Yes (none of the studies
-			No (excluded				Unclear	Unclear (funnel	
-			No (excluded studies not				Unclear (different	Unclear (funnel plot not	the studies
-			No (excluded studies not				Unclear (different definitions of	Unclear (funnel plot not provided for	the studies were
-			No (excluded studies not				Unclear (different definitions of PC-AKI used	Unclear (funnel plot not provided for subanalysis,	the studies were sponsored by

1. Research question (PICO) and inclusion criteria should be appropriate and predefined

2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched

3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons

4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported

5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)

6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)

7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?

8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)

Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up?⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year)		(unlikely/likely/un clear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncl ear)	(unlikely/likely/uncle ar)
Shehata, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Qiao, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Abaci, 2015	Not described	unclear	Unlikely	Unlikely	Unlikely	unlikely	Unclear	unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments
reference	characteristics			control (C)		effect size	
Liu, 2015	SR and meta-	Inclusion criteria SR:	Describe intervention:	Describe control:	End-point of follow-up	Outcome measure-1: PC-	Facultative:
	analysis of RCTs	RCTs investigating the			<u>(PC-AKI)</u> :	AKI, defined as an	

[individua		efficacy of statins in	A: Simvastin 40mg, 12	A: Placebo	A: within 48h after	increase of ≥25%SCr or	The result presented here
l study	Literature search	preventing CIN	hours for 2 days,	A. FIACEDO	contrast administration	SCr ≥0.5mg/dL within 48-	involves a subgroup
characteri	up to Feb 2014	compared with	80mg before		B: within 5 days	120h.	analyses of patients with
stics	up to Feb 2014	placebo, the treatment	procedure, 80mg after		C : 48h after PCI	12011.	impaired kidney function.
deduced	A : Jo, 2008	groups received statins	the procedure		D : 48h after from baseline	Effect measure: RR (95%	impaired kidney function.
		before the contrast		B: Oral NAC		-	The results of the study of
from [1st	B : Toso, 2010		B: Atorvastatin		value	CI:	The results of the study of
author,	C : Patti, 2011	exposure at any dose,	80mg/d for 48 hours	1200mg 2 times	E: within 72h after	A: 0.75 (0.17;3.28)	Quintavalle, 2012 are
year of	D: Quintavalle,	for any length of time.	before and after the	day before to the	contrast administration	B : 0.94 (0.48;1.83)	adapted (secondary
publicatio	2012	Studies were only	procedure versus	day after	F: within 72h after	C : 0.56 (0.21;1.47)	outcome measure is the
n	E: Han, 2013	included if none of the	placebo, oral NAC	procedure	contrast administration	D : 0.44 (0.17;1.13)	correct PC-AKI definition)
]]	F: Leoncini, 2013	arms or both received	1200mg 2 times day			E: 0.82 (0.33;2.04)	
		N-acetylcysteine.	before to the day		<u>For how many</u>	F : 0.41 (0.20;0.85)	Liu, 2015 include a fixed
PS., study	Study design:		after procedure		participants were no		analyses, the use of
characteri	RCT [parallel]	Exclusion criteria SR:	C: Atorvastatin 80 mg	C: Placebo	complete outcome data	Pooled effect (fixed	random analyses might
stics and		Trials comparing 2	12 hours before and		available?	effects model): 0.51	be preferred given the
results	Setting and	different doses of	further 40mg 2 hours		Not reported	(0.37;0.70) favouring	heterogeneity found
are	Country:	statins. Only studies	before angiography			intervention. I ² =44%	(I ² =44%)
extracted	Not reported	that included patients	D: 80mg within 24h	D: Placebo, oral			
from the		with renal dysfunction	before exposure, oral	NAC 1200mg ²		Outcome measure-2:	For the outcome
SR (unless	Source of	(defined as eGFR≤60	NAC 1200mg ²	times/day before		Mortality (cases)	measures mortality, start
stated	funding:	mL/min/1.73m ² or	times/day before and	and the day of		A: intervention=0,	of dialysis and ICU
otherwise	None was	creatine clearance ≤60	the day of procedure	procedure		placebo=0	admission, data
)	sponsored by	mL/min/1.73m ²) were	E: Rosuvastatin 10mg			B : intervention=1,	extraction took place
-	industry	included here.	from 2 days before to			placebo=0	using the original articles
	,		3 days after	E: placebo		C : NR	of the studies included in
		6 studies included	procedure			D: NR	Liu, 2015.
			F: Rosuvastin 40mg			E: NR	-,
		Important patient	followed by 20mg/d,	F : oral NAC 1200		F: NR	
		characteristics at	oral NAC 1200 mg 2	mg 2 times/d			
		baseline:	times/d before and	before and day		Outcome measure-3:	
		<u></u> -	day after procedure	after procedure		Start dialysis	
		<u>N</u>	ady after procedure			A: intervention=0,	
		A: 236				placebo=1	
		B : 304				B : intervention=0,	
		C : 74				placebo=1	
		D : 410				C : NR	
		E : 450				D: NR	
						E: NR	
		F : 210					
		Constant of the second se				F: NR	
		Groups comparable at				Outcome measure-4: ICU	
		baseline? Unclear	1		1	(not reported in any of	

			the included studies)	

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1 This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

	•
n laboratory moderate mg daily) for 48 h infusion of CKD. (eGFR 30−<90 before PCI, in addition isotonic saline and control: 0 control: 0 creatinine of ≥0.5 mg/dL pretreatment	showing a benefit upon e high dose

r r		For overale					
		For example					
		age ± SD:					
		1: 55 (6)					
		C:57 (5)					
		Sex:					
		sex: I: 53% M					
		C: 56% M					
		C: 30% IVI					
		Contrast (mL) (mean± SD)					
		l: 274 (8)					
		C: 278 (11)					
		0.270 (11)					
		Contrast nephropathy risk					
		score (mean± SD)					
		l: NR					
		C: NR					
		Groups comparable at					
		baseline? yes, no					
		statistical significant					
		differences					
Qiao,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	follow-up:	Outcome measures and	
2015	RCT	1. Diabetic patients; 2.	(treatment/procedure	(treatment/proced	Between 48-72h after	effect size (include 95%Cl	
		Mild to moderate CKD,	/test):	ure/test):	procedure, up to 30 days.	and p-value if available):	
	Setting:	which was defined as					
	Hospital	estimated glomerular	The rosuvastatin	Received no	Loss-to-follow-up:	Incidence of PC-AKI	
		filtration rate (eGFR) 30 to	group received 10 mg	statins during the	Intervention: 0	(increase in serum	
	Country:	89 ml/min per 1.73 m2; 3.	everyday for at least	trial. All patients		creatinine of ≥0.5 mg/dL	
	China	Total CM administrated	48 hours before and	received	Control: 0	or an absolute increase of	
		dose of volume ≥ 100 ml.	72 hours after CM	intravenous		≥25% from baseline <48	
	Source of		administration.	hydration with	Incomplete outcome	or72h after contrast	
	funding: not	Exclusion criteria:		isotonic saline	<u>data</u> :	exposure)	
	reported, no	Pregnancy, lactation,		(0.9% sodium	No		
	conflicts of	Ketoacidosis, Lactic		chloride 1-1.5		Intervention group: 2/60	
	interest	acidosis, prior CM		ml/kg/hour for 3-		events, control group	
		administration within 7		12 hours before		2/60 events, p<0.05	
		days of study entry.		and 6-24 hours			
		Importantly, all patients		after the		Mortality, initiation of	
		who were recent statin		procedure).		dialysis and ICU-	
		users (with 14 days before				admission not specifically	

	1						1
		the procedure) were				reported, but no post	
		excluded.				procedural adverse	
		See article for a complete				events occurred.	
		overview of exclusion					
		criteria.					
		<u>N total at baseline</u> :					
		Intervention: 60					
		Control: 60					
		Important prognostic					
		<u>factors²:</u>					
		For example					
		age ± SD:					
		I: 62 (8)					
		C:62 (8)					
		Sex:					
		I: 68% M					
		С: 73% М					
		Contrast (mL) (mean± SD)					
		I: 204 (75)					
		C: 212 (85)					
		Contrast nephropathy risk					
		score (mean± SD)					
		I: NR					
		C: NR					
		Groups comparable at					
		baseline? Yes, average					
		eGFR 60 ml/min/1.73 m ²					
Abaci,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	follow-up:	Outcome measures and	All patients received
2015	RCT	Patients naïve to statins	(treatment/procedure	(treatment/proced	Between 48-72h after	effect size (include 95%Cl	intravenous hydration
		and scheduled for	/test):	ure/test):	angiography, 6 months	and p-value if available):	with isotonic saline
	Setting:	coronary angiography			and 1 year.		(14mL/kg/h, 0.9% sodium
	University	with EGFR between 30	Patients were given	No statin		Incidence of PC-AKI	chloride) for 12h before
	cardiology	and 60 mL/min/1.73m ² .	40mg rosuvastatin	treatment	Loss-to-follow-up:	(increase in serum	and 24h after contrast
	institute,		<24 h before coronary		Intervention: 7 (6%)	creatinine of ≥0.5 mg/dL	exposure.
	inpatients	Exclusion criteria:	, angiography and		Reasons unknown	or an absolute increase of	
I	institute,		<24 h before coronary	treatment	Intervention: 7 (6%)	creatinine of ≥0.5 mg/dL	
L	mpatients	<u>Exclusion enterna</u> .	a				

	Emergency coronary	hereafter 20mg/day		≥25% from baseline <48	Statistical analyses not
Country:	angiography, acute renal	for 2 days.	Control: 5 (5%)	or72h after contrast	clear. Secondary
Turkey	failure or end-stage renal		Reasons unknown	exposure.	outcomes (death and
	failure requiring dialysis.				decrease in eGFR of ≥25%
Source of	See article for a complete		Incomplete outcome	Intervention group: 6/103	or renal failure requiring
funding: not	overview of exclusion		<u>data</u> :	events, control group	dialysis at 12 months)
reported, no	criteria.		See loss to follow-up	9/105 events. Relative	were reported as a
conflicts of				risk (95%Cl)= 0.71 (0.25;-	composite outcome and
interest	N total at baseline:			2.0)	exact data was not
	Intervention: 110				shown.
	Control:110			Mortality, initiation of	
				dialysis and ICU-	
	Important prognostic			admission not reported	
	factors ² :				
	For example				
	age ± SD:				
	I: 67.5 (8.9)				
	C:67.7 (8.9)				
	Sex:				
	1: 64% M				
	С: 73.4% М				
	Contrast (mL) (mean± SD)				
	<i>I: 139.2 (77.4)</i>				
	C: 117.7 (56.8)				
	C. 117.7 (50.8)				
	Contrast nephropathy risk				
	score (mean± SD)				
	<i>I: 9.3 (3.9)</i>				
	C: 7.7 (3.4)				
	0.777 (0.77				
	Groups comparable at				
	baseline? Not completely,				
	see contrast volume and				
	contrast nephropathy risk				
	(above)				

Notes:

1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures

- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	131
(OVID)	(112282)	
	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or	
1995-aug.	nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
2015	(536907)	
	3 1 and 2 (8955)	
Engels,	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
	ciaki).ti,ab. (1969)	
Nederlands	5 3 or 4 (9449)	
	6 limit 5 to (yr="1995-Current" and (dutch or english)) (5521)	
	7 exp hydroxymethylglutaryl-coa reductase inhibitors/ or (statin* or lovastatin* or	
	meglutol* or pravastatin* or simvastatin* or rosuvastatin* or	
	atorvastatin*).).ti,ab,kw. or (hydroxymethylglutaryl* adj4 inhibitor*).ti,ab,kw.	
	(45277)	
	8 6 and 7 (131)	
	9 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic*	
	or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review	
	Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab.	
	or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection	
	criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or	
	Letter/ or (animals/ not humans/)) (248141)	
	10 8 and 9 (32) – 31 uniek	
	11 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or	
	randomized controlled trials as topic/ or Random Allocation/ or Double-Blind	
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or	
	clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or	
	randomized controlled trial or multicenter study or clinical trial).pt. or	
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj	
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/)	
	(1508278)	
	12 8 and 11 (71)	
	13 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or	
	Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or	
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or	
	(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or	
	prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically	
	controlled study/ or interrupted time series analysis/ [Onder exp cohort studies	
	vallen ook longitudinale, prospectieve en retrospectieve studies] (2209511)	
	14 8 and 13 (38)	
	15 12 not 10 (45)	
	22 (12 or 14) not 10 (58) – 56 uniek	
Fuchase	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2	
Embase	(nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR	
(Elsevier)	(contrast medium/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3	
	medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2	
	(disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2	
	(insufficienc* OR function* OR disease* OR failure*)):ab,ti))	
	(insufficience of function of disease of failure)).ab,(i))	
	AND ("hydroxymathylglutaryl coopyyme a reductace inhibitor" (ovn (mi OB	
	AND ('hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp/mj OR statin*:ab,ti OR lovastatin*:ab,ti OR meglutol*:ab,ti OR pravastatin*:ab,ti OR	
	simvastatin*:ab,ti OR rosuvastatin*:ab,ti OR atorvastatin*:ab,ti OR	
	(hydroxymethylglutaryl* NEAR/4 inhibitor*):ab,ti)	
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [1995-2015]/py	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR	
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1	
	analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR	
	'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR	
	'nonhuman'/exp NOT 'human'/exp)) (34) – 6 uniek	
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR	
		I
	'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR	
	'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR	

Appendices to chapter 7.2

Evidence tables

Table: Exclusion after i	
Author and year	Reason for exclusion
ACT Investigators,	description of study design, not an original article
2009	
Amini, 2009	Prehydration only, not comparable to Dutch clinical practice
Ashworth, 2010	overlaps with Loomba, 2013 and is a less recent review
Azmus, 2005	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Bagshaw, 2006	review, not systematic
Berwanger, 2012	Sub-analysis of ACTT studty (which is already included in literature analysis)
Briguori, 2011	Does not compare N-acetylcysteine to placebo
Briguori, 2007	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Brown, 2009	overlaps with Loomba, 2013 and is a less recent review
Burns, 2010	Not specifically patients with normal or abnormal kieny function (mix of impaired kidney
	function and diabetics)
Busch, 2013	overlaps with Loomba, 2013 and is a less recent review
Buyukhatipoglu,	outcome measures as described in PICO not reported
2010	
Calabro, 2011	observational study
Carbonell, 2010	already included in Loomba 2013, and Sun, 2013
Carbonell, 2007	already included in Loomba 2013, and Sun, 2013
Chen, 2008	does not compare no NAC to NAC (both treatment arms recieve NAC)
Coyle, 2006	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Duong, 2005	overlaps with Loomba, 2013 and is a less recent review
Gomes, 2005	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Gonzales, 2007	overlaps with Loomba, 2013 and is a less recent review
Gouveira, 2015	review, not systematic
Gulel, 2005	already included in Loomba 2013
Gurm, 2011	Does not answer study question
Hafiz, 2012	Acetylcysteine not compared to control
Hassan, 2011	observational study
Housseinjani, 2013	review, not systematic
Hsu, 2012	already included in review Wu 2013
Hsu, 2007	already included in review Wu 2013
Izcovich, 2015	systematic review, poor quality (no clear description of included studies)
Jo, 2009	does not compare no NAC to NAC
Juergens, 2010	does not compare no NAC to NAC (both treatment arms recieve NAC)
Khalili, 2006	Prehydration only, not comparable to Dutch clinical practice
Kim, 2010	already included in Loomba 2013
Kotlyar, 2005	Dubbel met Kotlyar, 2005
Lee, 2011	does not compare no NAC to NAC (both treatment arms recieve NAC)
Liu, 2006	overlaps with Loomba, 2013 and is a less recent review
Marenzi, 2006	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Mittal, 2014	review, not systematic
Momeni, 2012	Observational study
O'Sullivan 2013	Does not answer reseach question broadly enough, used for cross refernecing
Ratcliffe, 2009	Not specifically patients with normal or abnormal kidney function (mix of impaired
	kidney function and diabetics)
Ritz, 2006	letter to the editor, not an original article
Sandhu, 2006	Unclear if patients were hydrated next to the NAC administration or not
Sar, 2010	Not specifically patients with normal or abnormal kidney function (mix of impaired
541, 2010	Hor specifically patients with format or abilitinal kidney function (fink or impailed

Table: Exclusion after revision of full text

	kidney function and diabetics)			
Shabbir, 2015	Article not found			
Shalansky, 2006	Shalansky, 2006 review, not systematic			
Solomon, 2014 review, not systematic				
Staniloae, 2009	Staniloae, 2009 subanalysis of trial, observational data			
Thiele, 2010	hiele, 2010 already included in Loomba 2013			
Trivedi, 2009	rivedi, 2009 overlaps with Loomba, 2013 and is a less recent review			
Zagler, 2006	Zagler, 2006 overlaps with Loomba, 2013 and is a less recent review			

Risk of bias table for intervention studies (randomized controlled trials) Research question:

Study reference (first author, publicatio	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ² (unlikely/likely/	Bias due to inadequate blinding of participants to treatment allocation? ³ (unlikely/likely/uncl	Bias due to inadequate blinding of care providers to treatment allocation? ³ (unlikely/likely/uncle	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³ (unlikely/likely/uncl	Bias due to selective outcome reporting on basis of the results? ⁴ (unlikely/likely/un	Bias due to loss to follow-up? ⁵ (unlikely/likely/uncle	Bias due to violation of intention to treat analysis? ⁶ (unlikely/likely/uncle
n year)		unclear)	ear)	ar) CT scan, normal kid	ear)	clear)	ar)	ar)
Hsu, 2012	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
				CT scan, decreased k	idney function			
Kama, 2014	By website randomization.c om	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Kitzler, 2012	Not reported	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear	Unclear
Poletti, 2007	Randomized by serial enrolment	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Poletti, 2013	Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
Tepel, 2000	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unlikely
				CAG or PCI, normal k	kidney function			
Carbonell, 2007	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Jaffery,	"Randomly	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Unlikely	Unclear

2012	assigned"							
Kim, 2010	Computer- generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Kinbara, 2010	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Lawlor, 2004	"randomization was performed by the hospital clinical trials pharmacist"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Sadat, 2011	Computer generated randomization scheme	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Tanaka, 2011	"Randomly assigned"	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Thiele, 2010	Computer generated random numbers	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
				CAG or PCI, deci	reased kidney function			
ACT, 2011	24-hour Web- based automated randomization system	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely
Castini, 2010	Computer generated randomization table	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Ferrario, 2009	Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Gulel,	Random	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear

2005	allocation table							
Habib, 2016	Patients were randomized into three groups	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Izani Wan (Mohame d), 2008	Computer generated randomization list	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Koc, 2012	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Kotlyar, 2005	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Sadineni, 2017	Patients were randomly assigned	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear
Seyon, 2007	Not described	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear	Unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1 This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study	Study	Patient characteristics ²	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments				
reference	characteristic			control (C) ³		effect size ⁴					
	S										
	CT scan, normal kidney function										
Hsu, 2012	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:				
	Randomized	1) all adult patients who	intervention	(treatment/proced	72 hours	effect size (include 95%Cl	A singe dose of NAC				
	controlled	received chest or	(treatment/procedu	ure/test):		and p-value if available):	before CECT imagingcan				
	trial	abdominal contrast-	re/test):				prevent CIN in an ED				
		enchanced computed		0.9% sodium	Loss-to-follow-up:	CIN05:	setting. However it does				
	Setting:	tomography (CECT)	600mg NAC	chloride (3	Not reported	(=a rise in SCr ≥0.5mg/dL	not improve mortality				
	emergency		In 0.9% sodium	mL/kg/h) for 60		within 48-72 hours after	rate or the need for				
	department,	Exclusion criteria:	chloride (3 mL/kg/h)	minutes prior to	Incomplete outcome	CECT imaging)	dialysis.				
	medical	1) patients undergoing	for 60 minutes prior	the CECT	<u>data</u> :	I: 7.5%					
	teaching	long-term hemodialysis or	to the CECT		Not reported	C: 14.6%	Patients with congestive				
	center	peritoneal hemodialysis		0.9% sodium		Odds Ratio (OR): 0.31	pulmonary edema				
		patients who received	0.9% sodium	chloride (1		(95% CI: 0.10 – 0.96,	received an adjusted				
	Country:	another dose of contrast	chloride (1 mL/kg/h)	mL/kg/h) for 6		p=0.04)	hydration schedule				
	Taiwan	medium within 72 hours	for 6 hours after	hours after CECT			where the rates of fluid				
		patient refused to sign	CECT			CINor:	loading were decreased				
	Source of	concent forms				(=a rise in SCr ≥0.5mg/dL	by 50%.				
	funding: non-	patients had a knon				or 25% within 48-72					
	commercial	allergic reaction to N-				hours after CECT imaging)					
		acetlycysteine (NAC)				I: 11.3%					
						C: 19.4%					
		N total at baseline:				OR: 0.35 (95% CI: 0.13 –					
		Intervention: 106				0.91, 0=0.03)					
		Control: 103									
						Mortality:					
		Important prognostic				I: 7.5%					
		<u>factors</u> ² :				C: 12.6%					
		For example				OR: 0.49 (95% CI: 0.15 –					
		age ± SD:				1.55, p=0.22)					

	I: 80 ± 9 C: 80 ± 11 Sex: I: 74% M C: 76% M Baseline SCr (mg/dL) ± SD I: 1.40 ± 0.58 C: 1.26 ± 0.43 Groups comparable at baseline?		an decreased kidney f	instign	Permanent renal replacement therapy: 0% in both groups	
Kama Tuna of study	Inclusion esiteria.		an, decreased kidney f		Outeene meesure and	Authons' conclusion.
Kama, 2014Type of study: randomized controlled trialSetting: emergency department, academic tertiary hospitalCountry: TurkeySource of funding: not reported	Inclusion criteria: 1) adult patients (≥18 years) who presented to the emergency department 2) patients who received CECT as part of their emergency care 3) moderate or high risk for contrast induced nephropathy (CIN) according to Mehran score (>5) Exclusion criteria: 1) CIN risk determine as Low by Mehran score 2) history of contrast- related allergies 3) hemodynamically unstable patients requiring resuscitation or surgery 4) patients receiving renal replacement therapy 5) patients did not provide	Describe intervention (treatment/procedu re/test): 150mg/kg NAC In 1000mL in 0.9% saline at the rate of 350ml/hour for 3 hours Before, after and during administration of contrast	Describe control (treatment/proced ure/test): 1000mL 0.9% saline at the rate of 350ml/hour for 3 hours Before, after and during administration of contrast	Length of follow-up: 48-72 hours Patients who were diagnosed with CIN – 1 months Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): CIN (=25% increase or greater than 0.5mg/dL (44µmol/L) increase in the serum creatinine level, 48-72 hours after administration of the contrast agent compared with the baseline creatinine measurement) I: 7 (19%) C: 5 (14%) p>0.05 No contrast- or treatment-induced adverse events were detected during emergency department care	Authors' conclusion: None of the short-term protocols with normal saline or NAC was superior in the emergency department pateints requiring CECT who had a moderate or high risk of CIN.

		infomed consent					
		intollica consent					
		N total at baseline:					
		Intervention: 36					
		Control: 35					
		Important prognostic					
		factors ² :					
		For example					
		age (95% CI):					
		1: 69 (65-73)					
		C: 67 (62-72)					
		Sex:					
		1:69 % M					
		C: 65% M					
		eGFR <20 mL/min/1.73m ²					
		I: 25%					
		C: 9%					
		eGFR 40-20					
		mL/min/1.73m ²					
		1: 36% C: 46%					
		eGFR 60-40mL/min/1.73m ²					
		l: 11%					
		C: 14%					
		Groups comparable at					
		baseline? Yes					
Kitzler,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2012	randomized	-patients with chronic	intervention	(treatment/proced	Not reported	effect size (include 95%Cl	Following radiocontrast
	controlled	kidney disease stage 1-4	(treatment/procedu	ure/test):	Loss to follow up:	and p-value if available):	administration neither
	trial	undergoing elective	re/test):	0.45% coline	Loss-to-follow-up:	No patients developed	vitamin E nor NAC in
	Setting:	computer-assisted tomography with non-ionic	N-acetylcysteine	0.45% saline, 1mL/kg/h over 24	Not reported	No patients developed contrast induced acute	addition to saline demonstrated an
	single-center,	radiocontrast agents when	4800mg per os	hours	Incomplete outcome	kidney injury.	additional beneficial
	single-center,	radiocontrast agents when		110013	incomplete outcome	Kiuncy injury.	

	elective	compared to 0.45% saline			data:		effect on kidney
	patients	alone	0.45% saline,		Not reported	There was no significant	fi=unction when
			1mL/kg/h over 24			difference in serum	compared to saline alone.
	Country:	Exclusion criteria:	hours			creatinine change	·
	,	-				between the three study	
	Source of					arms.	
	funding:	N total at baseline:					
	Ū.	Intervention: 10					
		Control: 10					
		Important prognostic factors ² : For example age ± SD: mean: 75 years					
		(not reported per group)					
		Sex:					
		38% M					
		(not reported per group)					
		Groups comparable at					
		baseline? Unc;ear					
Poletti,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2007	randomized	1) patients admitted	intervention	(treatment/proced	4 days	effect size (include 95%Cl	
	controlled	consecutively to the	(treatment/procedu	ure/test):		and p-value if available):	On the basis of the serum
	trial	emergency department	re/test):		Loss-to-follow-up:	Nephrotoxicity	creatinine concentration,
		during daytime hours		placebo in 5%	7 (8%)	(=≥25% increase in serum	iv administration of NAC
	Setting:	2) serum creatinine	900mg NAC diluted	glucose solution	3 died, 3 left hospital 1	creatinine value)	appears protective
	emergency	>1.2md/dL	in 5% glucose	administered iv 1	transferred to another	I: 2/44 (5%)	against the
	patients		solution	hour before CT	hospital (not reported	C: 9/43 (21%)	nephrotoxicity of
		Exclusion criteria:	administered iv 1		per group)	P=0.026	contrast medium.
	Country:	1) pregnancy	hour before CT	0.45% saline iv at a			
	Switzerland	end stage renal failure		rate of 5mL/kg	Incomplete outcome		
		with dialysis	0.45% saline iv at a	body weight over	<u>data</u> :		
	Source of	suspicion of acute renal	rate of 5mL/kg body	the course of an	As above		
	funding: not	obstruction	weight over the	hour before CT			
	reported	4) asthma	course of an hour				

		5) severe cardiac failure 6) hemodynamically unstable condition contraindicating iv hydration 7) nonurgent indications for CT <u>N total at baseline</u> : 87 Intervention: 44 Control: 43 <u>Important prognostic</u> <u>factors²</u> : <i>For example</i> <i>age ± SD</i> : <i>I: 70 ± 19</i> <i>C: 73 ± 17</i> <i>Sex:</i> <i>I: 59% M</i> <i>C: 67% M</i> Groups comparable at baseline? Yes	before CT 900mg NAC mixed into the 0.45% saline perfusion administered iv after completion of CT at a rate of 1mL/kg body weight per hour for 12 hours	placebo mixed into the 0.45% saline perfusion administered iv after completion of CT at a rate of 1mL/kg body weight per hour for 12 hours			
Poletti,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2013	randomized controlled	1) patients admitted consecutively to the	intervention (treatment/procedu	(treatment/proced ure/test):	10 days	effect size (include 95%Cl and p-value if available):	An ultra-high dose of
	trial	emergency department	re/test):		Loss-to-follow-up:		intravenous NAC is
		2) estimated creatinine	. ,	placebo diluted in	Intervention:	Nephropathy	ineffective at preventing
	Setting:	clearance by MDRD of	6000mg NAC iv	100mL saline,	3 (5%)	(=increase of at least 25%	nephrotoxicity in patients
	emergency	<60ml/min/1.73m ²	diluted in 100mL	administered in the	Reasons not reported	or 44µmol/l in serum	with renal impairment
	department patients	Exclusion criteria:	saline, administered in the 60 minutes	60 minutes before the CT-scan	Control:	creatinine level at day 2,4 or 10 compared to day 0)	undergoing emergency contrast CT.
	patients	1) asthma	before the CT-scan		1 (2%)	l: 8 (15%)	Contrast CT.
	Country:	2) pregnancy		Hydration of	Reasons not reported	C: 10 (17%)	
	Switzerland	3) obstructive nephropathy	Hydration of 250mL	250mL of 0.45%		P=0.99	

			(o 1=o/)				
		patient's refusal	of 0.45% saline	saline before CT-	Incomplete outcome		
	Source of		before CT-scan	scan	<u>data</u> :	Composite event of death	
	funding: not	<u>N total at baseline</u> : 104			As above	or acute kidney injury	
	reported	Intervention: 55	1000mL saline	1000mL saline		I: 33%	
		Control: 59	0.45% after CT-scan	0.45% after CT-		C: 24%	
				scan		p-value not reported	
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		<i>I: 78 ± 12</i>					
		C: 78 ± 12					
		Sex:					
		I: 49% M					
		C: 51% M					
		0.01/0/11					
		Groups comparable at					
		baseline? Yes					
Tepel,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2000	Randomized	1) patients with a serum	intervention	(treatment/proced	48 hours, 6 days	effect size (include 95%Cl	Authors conclusion.
2000	controlled	creatinine >1.2mg/dL or	(treatment/procedu	ure/test):	40 Hours, 0 duys	and p-value if available):	Prophylactic
	trial	creatinine clearance	re/test):	urc/testj.	Loss-to-follow-up:		administration of the
	tilai	<50mL/min		Saline (0.45%) iv.	Not reported	Increase of at least	antioxidant
	Setting:	2) known chronic renal	Acetylcycsteine	1ml/kg/h for 12	Not reported	0.5mg/dL (44µmol/L) in	acetylcysteine, along with
	elective	failure and a stable serum		hours before and		serum creatinine	
		creatinine concentration	orally 600mg twice daily on the day	12 hours after	Incomplete outcome	concentration 48 hours	hydration, prevents the reduction in renal
	patients		, ,		data:		
	receiving CT-	3) patients receiving	before and on the	contrast	Not reported	after administration of	function induced by
	scan at	elective CT-scans	day of	administration		contrast agent:	iopromide, a non-ionic,
	hospital		administration of			I: 1/41 (2%)	low-osmolality contrast
		Exclusion criteria:	the contrast agent			C: 9/42 (21%)	agent, in patients with
	Country:	1) acute renal failure				RR: 0.1 (95% CI: 0.01 –	chronic renal
	Germany		Saline (0.45%) iv.			0.9)	insufficiency.
		N total at baseline:	1ml/kg/h for 12			P=0.01	
	Source of	Intervention: 41	hours before and 12				
	funding: not	Control: 42	hours after contrast			None of the patients	
	reported		administration			required dialysis	

	Important prognostic factors ² : For example age ± SD: 1: 66±11 C: 65 ± 15 Sex: 1:59 % M C: 55% M Groups comparable at baseline? Yes					
	Dusenne: 163	CAG	l or PCI, normal kidney f	function		<u> </u>
Carbonell , 2007 Type of study: randomized controlled trial Setting: tertiary hospital, cardiac unit Country: Spain Source of funding: not reported	Inclusion criteria:1) patients with acutecoronary syndrome andnormal renal function,admitted to the cardiacunit and referred forcardiac catheterization2) angina at rest or post-myocardial infarctionOr they had receivedthrombolytic therapy withfailed recanalization so thecardiac catheterisation wasan emergency procedureExclusion criteria:1) chronic renal failure oracute renal dysfunction2) hemodynamic instability(systolic blood pressure<90mmHg)	Describe intervention (treatment/procedu re/test): NAC (600mg diluted in 50mL of 0.9% saline) iv for 30 minutes twice daily for a total of 4 times Starting at least for 6 hours before the administration of contrast media 0.9% saline iv at least 6 hours before procedure, maintained for 12 hours after contrast dosing	Describe control (treatment/proced ure/test): placebo (diluted in 50mL of 0.9% saline) iv for 30 minutes twice daily for a total of 4 times Starting at least for 6 hours before the administration of contrast media 0.9% saline iv at least 6 hours before procedure, maintained for 12 hours after contrast dosing	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): Contrast induced nephropathy (=an acute increase in the serum creatinine concentration ≥0.5mg/dL and/or >25% increase above baseline level at 48 hours after contrast dosing) I; 10.3% C: 10.1% P=0.50 None of the patients required dialysis.	Patients with congestive heart failure received a reduced hydration volume. Authors' conclusion: The prophylactic administration of intravenous NAC provides no additional benefit to saline in high-risk coronary patients with normal renal function.

		4) untreated					
		gastrointestinal bleeding					
		5) previous treatment with					
		theophylline, mannitol or					
		nephrotoxic antibiotics					
		N total at baseline:					
		Intervention: 107					
		Control: 109					
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		1: 63 ± 14					
		C: 61 ± 12					
		Sex:					
		I: 80% M					
		С: 73% М					
		Creatinine clearance					
		(ml/min)					
		1: 86 ± 29					
		C: 88 ± 30					
		Groups comparable at					
		baseline?					
Jaffery,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Patients with clinical
2012	randomized	1) patients hospitalized	intervention	(treatment/proced	72 hours for lab	effect size (include 95%Cl	evidence of heart failure
	controlled	with a primary diagnosis of	(treatment/procedu	ure/test):	parameters	and p-value if available):	received only NAC iv or
	trial	acute coronary syndrome	re/test):		30 days for mortality and		placebo
		2) scheduled for coronary			hospital stay	CIN	
	Setting:	angiography (CAG) or		Placebo in 500ml		(=increase in serum	Authors' conclusion:
	single-center	intervention during this	NAC: 1200mg bolus	5% dextrose	Loss-to-follow-up:	creatinine concentration	In acute coronary
	inpatients,	hospitalization	followed by	solution of water iv	Not reported	≥25% above the baseline	syndrome patients
	emergency	age ≥18 years	200mg/h for 24			level within 72 hours of	undergoing CAG with or

	procedure		hours	Normal saline	Incomplete outcome	the administration of	without poroutopoout
	procedure	Evelveien eriterie.	hours		Incomplete outcome		without percutaneous
	Country	Exclusion criteria:	In 500ml 5%	(0.9%) iv; 1/ml/kg for 24 hours	data:	intravenous contrast)	intervention (PCI), high- dose intravenous NAC
	Country:	1) end stage renal disease		for 24 nours	Not reported	l: 16%	
	United States	requiring dialysis	dextrose solution of			C:	failed to reduce the
	of America	2) hypersensitivity to NAC	water iv			13%	incidence of CIN.
	a a	3) history of life-				P=0.40	
	Source of	threatening contrast	Normal saline				
	funding: not	reaction	(0.9%) iv; 1/ml/kg			Outcomes of mortality	
	reported		for 24 hours			and length of hospital not	
		N total at baseline:				reported.	
		Intervention: 192					
		Control: 206					
		lasa atau tana ana ata					
		Important prognostic					
		<u>factors</u> ² :					
		For example					
		age ± SD:					
		1: 66 ± 13					
		C: 65 ± 13					
		Sex:					
		I: 67 % M					
		C: 59 % M					
		C. 35 /0 WI					
		Baseline creatinine					
		clearance (ml/min)					
		1: 87 ± 41					
		$C: 92 \pm 44$					
		Groups comparable at					
		baseline? Yes					
Kim, 2010	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
	randomized	1) patients scheduled for	intervention	(treatment/proced	48 hours	effect size (include 95%CI	
	controlled	elective CAG and/or PCI	(treatment/procedu	ure/test):		and p-value if available):	Not relevant – based on
	trial	with apparently normal	re/test):		Loss-to-follow-up:		cystatin-C defined CIN
		renal function		0.9% saline	Not reported	CIN	results and not the sCR
	Setting:		Oral acetylcysteine	1/mL/kg/h for 12		(=increase in sCR of at	based CIN.

]
elective	Exclusion criteria:	600mg twice a day	hours before and	Incomplete outcome	least 0.5mg/dL or >25%	
patients, one	1) acute coronary	on the day before	6hours after CAG	data:	within 48 hours of	
hospital	syndrome requiring	and the day of		Not reported	contrast exposure)	
	emergency CAG/PCI	coronary			I: 3.8%	
Country:	2) cardiogenic shock	angiography			C: 8.1%	
South Korea	iodinated contrast				p>0.05	
	media administration	0.9% saline				
Source of	within a monthor NAC	1/mL/kg/h for 12				
funding: not	within 48 hours before	hours before and				
reported	study entry	6hours after CAG				
	4) current dialysis or a					
	serum creatinine					
	>1.4mg/dL for men or					
	>1.2mg/dL for women					
	5) thyroid diseases					
	6) allergy to the study					
	medication					
	medication					
	N total at baseline:					
	Intervention: 80					
	Control: 86					
	control. so					
	Important prognostic					
	factors ² :					
	For example					
	age ± SD:					
	l: 62 ± 11					
	$C: 62 \pm 10$					
	$C: 62 \pm 10$					
	Com					
	Sex:					
	1: 79% M					
	C: 67% M					
	SCr (mg/dL)					
	I: 1.03 ± 0.17					
	C: 1.03 ± 0.14					

		Groups comparable at baseline? Yes					
2010	Type of study: randomized controlled trial Setting: elective patients, one hospital Country: Japan Source of funding: not reported	Inclusion criteria: 1) Patients with stable coronary artery disease scheduled to undergo CAG and/or PCI, with stable serum creatinine concentrations Exclusion criteria: 1) acute myocardial infarction 2) use of vasopressors before PCI 3) cardiogenic shock 4) current peritoneal or hemodialysis 5) planned post-contrast dialysis 6) allergies to ths study medications 7) congestive heart disease 8) severe valvular disease 8) severe valvular disease 9) pregnancy 10) multiple myeloma 11) amyloidosis <u>N total at baseline</u> : Intervention: 15 Control: 15 <u>Important prognostic</u> factors ² : For example age ± SD: 1: 70 ± 10	Describe intervention (treatment/procedu re/test): NAC 704mg orally twice daily on the day before ond on the day of CAG and/or PCI 0.9% saline iv 1/ml/kg/hour For 30 minutes before and 10 hours after angiography	Describe control (treatment/proced ure/test): 0.9% saline iv 1/ml/kg/hour For 30 minutes before and 10 hours after angiography	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): CIN (=SCr increase of >0.5mg/dL from baseline to 48 hours to angiography) I: 0 (0%) C: 4 (27%) 96% CI: 0.10 – 5.991, p=0.011	Authors' conclusion: These results suggest that both prophylactic NAC and aminophylline administration are effective in preventing CIN, but not with hydration alone.

	C: 70 ± 8 Sex: I: 80% M C: 80% M SCr (mg/dL) I: 1.00 ± 0.36 C: 0.94 ± 0.21					
	Groups comparable at					
Lawlor, 2004 Type of stur randomized controlled trial Setting: elective patients, single cente Country: United Kingdom Source of funding: no reported	 1) patients with peripheral vascular disease going for elective angiography or angioplasty to participate in this trial Exclusion criteria: <u>N total at baseline</u>: Intervention: 46 Control: 48 Important prognostic 	Describe intervention (treatment/procedu re/test): 1g of NAC in each bag of 0.9% saline 0.9% saline (500mL over 4-6 hours) 6-12 hours prior to angiography and again after angiography	Describe control (treatment/proced ure/test): 0.9% saline (500mL over 4-6 hours) 6- 12 hours prior to angiography and again after angiography with placebo	Length of follow-up: 7 days Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): CIN (=a rise of 25% or 0.5mg/dL in sCR at 48 hours after contrast administration) Patients with normal kidney function: I: 0/29 (0%) C: 0/27 (0%) p>0.05 Patients with decreased kidney function: I: 3/17 (18%) C: 3/21 (14%) p>0.05	Authors' conclusion: NAC pre-contrast and post-contrast does not confer any benefit in preventing radiocontrast induced nephropathy in vascular patients

		SCr (μ mol/L) I: 110 ± 42 C: 124 ± 63 Groups comparable at baseline? Yes					
Sadat, 2011	Type of study: randomized controlled trial Setting: elective patients, single center Country: United Kingdom Source of funding: no funding	Inclusion criteria: 1) patients undergoing peripheral angiography for peripheral artery disease Exclusion criteria: 1) patients with established renal failure – on renal replacement therapy N total at baseline: Intervention: 21 Control: 19 Important prognostic factors ² : For example age ± SD: I: 75 ± 11 C: 70 ± 14 Sex: Not reported Groups comparable at baseline? Unclear	Describe intervention (treatment/procedu re/test): NAC 600mg twice daily orally on the ay before and on the day of CAG (2.4g in total) Iv hydration 0.9% saline 1L over 12 hours before CAG 1L over 12 hours after CAG	Describe control (treatment/proced ure/test): Iv hydration 0.9% saline 1L over 12 hours before CAG 1L over 12 hours after CAG	Length of follow-up: 72 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=0.5mg/dL or 25% increase in sCr from baseline value within 48 hours of exposure to intravascular radiographic contrast media that is not attributable to other causes) I: 1/21 (5%) C: 3/19 (16%) P=0.33	Authors' conclusion: A clear conclusion is not formulated.
Tanaka, 2011	Type of study: randomized controlled trial	Inclusion criteria: 1) patients admitted for ST- segment elevation acute myocardial infarction	Describe intervention (treatment/procedu re/test):	Describe control (treatment/proced ure/test):	Length of follow-up: 36 hours Loss-to-follow-up:	Outcome measures and effect size (include 95%Cl and p-value if available):	Authors' conclusion: While N=acetylcysteine might have the possibility

		treated with primary PCI			Not reported	CIN	to reduce the incidence
	Setting:			Hydration with iv		(=an increase in sCr level	of contrast-induced
	emergency	Exclusion criteria:	NAC 705mg orally	Ringer lactate	Incomplete outcome	of 25% or more from	nephropathy in patients
	patients,	1) dialysis	before and 12, 24,	solution at a rate of	data:	baseline value within 72	undergoing primary
	single center	2) known allergy to NAC	26 pours after	1-2ml/kg/hour for	Not reported	hours after primary	angioplasty for acute
	U U	3) inability to take NAC	intervention (2.8g in	more than 12		angioplasty)	myocardial infarction, the
	Country:	orally	total)	hours after primary		1: 2/38 (5%)	in-hospital mortality and
	Japan		,	CAG		C: 5/38 (13%)	morbidity were not
		N total at baseline:	Hydration with iv			P=0.21	significantly different
	Source of	Intervention: 38	Ringer lactate				between the two groups.
	funding: not	Control: 38	solution at a rate of			No major adverse events	<u> </u>
	reported		1-2ml/kg/hour for			(death, acute renal failure	
		Important prognostic	more than 12 hours			requiring temporary	
		factors ² :	after primary CAG			replacement therapy,	
		For example				need for mechanical	
		age ± SD:				ventilation) occurred in	
		I: 63 ± 13				either group during the	
		C: 61 ± 14				in-hospital follow-up	
						period.	
		Sex:					
		I: 82% M					
		С: 82% М					
		SCr (mg/dL)					
		I: 0.95 ± 0.34					
		C: 0.88 ± 0.25					
		Groups comparable at					
		baseline? Yes					
Thiele,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2010	randomized	1) patients with acute	intervention	(treatment/proced	Laboratory parameters:	effect size (include 95%Cl	
	controlled	myocardial infarction	(treatment/procedu	ure/test):	72 hours	and p-value if available):	High-dose iv NAC does
	trial	undergoing primary PCI	re/test):		Clinical endpoints: 6		not provide additional
		2) symptoms <12 hours			months	CIN	clinical benefit to placebo
	Setting:	and ST-segment elevation		10mL of 0.9%		(=increase in sCr of ≥25%	with respect to CIN in
	emergency	≥ 0.1 mV in ≥ 2 extremity	NAC intravenous	saline at each	Loss-to-follow-up:	from baseline within 72	non-selected patients
	patients, one	leads or ≥o.2 mV in ≥2 ore-	bolus	injection	none	hours after PCI)	undergoing angioplasty

tertiary hospita Country German Source funding reporte	I Exclusion criteria: y: 1) previous fibrinolysis <12 hy hours 2) known NAC allergy of 3) chronic dialysis y: not 4) pregnancy	Hydration with intravenous 0.9% saline; infusion rate 1ml/kg/hour for 12 hours (or 0.5mg/kg/h in overt heart failure)	Hydration with intravenous 0.9% saline; infusion rate 1ml/kg/hour for 12 hours (or 0.5mg/kg/h in overt heart failure)	Incomplete outcome data: none	I: 18/126 (14%) C: 25/125 (20%) P=0.28 Mortality after 6 months I: 12/126 (14%) C: 12/125 (14%) p>0.05 New congestive heart failure I: 11/126 (9%) C: 7/125 (6%) p>0.05	with moderate doses of contrast medium and optimal hydration.
			r PCI, decreased kidney			
ACT, 2011 Type of random		Describe intervention	Describe control (treatment/proced	Length of follow-up: 48-96 hours for	Outcome measures and effect size (include 95%Cl	Authors' conclusion

controlled	CAG or peripheral arterial	(treatment/procedu	ure/test):	laboratory parameters	and p-value if available):	In this large randomized
trial	angiography	re/test):		30 days for clinical events		trial we found that
	2) at least one risk factor				CI-AKI	acetylcysteine does not
Setting:	for CI-AKI:	NAC 2x600mg orally	placebo orally	Loss-to-follow-up:	(=a 25% elevation of sCr	reduce the risk of
inpatients,	-age >70 years	every 12 hours for 2	every 12 hours for	Intervention:	above baseline 48-986	contrast-induced acute
elective,	-chronic renal failure	days	2 days	56 (5%)	hours after angioplasty)	kidney injury or other
multi-centre	-diabetes mellitus	(2 doses before and	(2 doses before	12 did not receive study		clinically relevant
	-clinical evidence of	2 doses after	and 2 doses after	drug before angiography	All participants	outcomes in at-risk
Country:	congestive heart failure	contrast	contrast	15 were not submitted to	I: 147/1153 (12.7%)	patients undergoing
Brazil	-left ventricular ejection	administration, total	administration)	angiography	C: 142/119 (12.7%)	coronary or peripheral
	fraction <0.45	dose 4800mg)		19 were lost to 48-96	RR: 1.00 (95% CI: 0.81 –	vascular angiography.
Source of	-hypotension			hour serum creatinine	1.25, p=0.97)	
funding: non-		Hydration with 0.9%		follow-up		
commercial	Exclusion criteria:	saline 1mg/kg/hour	Hydration with	4 died before 48-96 hours	Patients with serum	
	-patients on dialysis	from 6-12 hours	0.9% saline	15 did not return to	creatinine >1.5mg/dL:	
	-patients with ST-segment	before to 6-12	1mg/kg/hour from	collect serum creatinine	I: 12/188 (6%)	
	elevation myocardial	hours after	6-12 hours before	1 was lost to 30-day	C: 10/179 (6%)	
	infarction	angiography	to 6-12 hours after	follow-up	P=0.75	
	-pregnancy or		angiography			
	breastfeeding			Control:	Patients with eGFR 30 –	
	-women <45 years who did			54 (5%)	60 mL/min	
	not use contraceptive			7 did not receive study	I: 30/425 (7%)	
	methods			drug before angiography	C: 27/398 (7%)	
				12 were not submitted to	RR: 1.04 (0.63 – 1.72)	
	N total at baseline:			angiography	P=0.73	
	Intervention: 1172			17 were lost to 48-96		
	Control: 1136			hour serum creatinine	Patients with	
				follow-up	eGFR<30ml/min	
	With eGFR<30 ml/min			3 died before 48-96 hours	I: 6/56 (11%)	
	I: 68			14 did not return to	C: 3/48 (6%)	
	C: 63			collect serum creatinine	RR: 1.71 (0.45 – 6.49)	
				1 was lost to 30-day	P=0.92	
	With eGFR 30 to 60 ml/min			follow-up		
	I: 515					
	C: 492					
				Incomplete outcome	Composite outcome of	
	Important prognostic			<u>data</u> :	death or need for dialysis:	

Castini, 2008	Type of study: randomized controlled trial Setting: elective patients, single centre Country: Italy Source of funding: not reported	factors ² :For exampleage ± SD:l: 68 ± 10C: 68 ± 10Sex:l: 62% MC:61 % MGroups comparable atbaseline? YesInclusion criteria:1) patients undergoingCAG and/or PCI2) age ≥18 years3) stable sCr ≥1.2mg/dLExclusion criteria:1) sCr >4mg/dL2) a history of dialysis,multiple myeloma,pulmonary edema,cardiogenic shock, acutemyocardial infarction3) emergencycatheterization4) recent exposure toradiographic contrastmedia within 7 days of thestudy	Describe intervention (treatment/procedu re/test): NAC 600mg orally every 12 hours for 2 days (2 doses before and 2 doses after contrast administration, total dose 2400mg) 0.9% saline iv 1ml/kg/hour for 12 hours before and 12 hours after contrast	Describe control (treatment/proced ure/test): 0.9% saline iv 1ml/kg/hour for 12 hours before and 12 hours after contrast administration	Intervention: 1153 (98%) had data included in laboratory parameters analysis 1171 (99.9%) had data included in secondary outcome analysis Reasons not reported Control: 1119 (98%) had data included in laboratory parameters analysis 1135 (99.9%) had data included in secondary outcome analysis Reasons not reported Length of follow-up: 5 days Loss-to-follow-up: none Incomplete outcome data: Not reported	I: 2,2% C: 2.3% Hazard ratio (HR): 0.97 (95% CI: 0.56 – 1.69, p=0.92) Cardiovascular deaths: HR: 0.99 (95% CI: 0.51 – 1.99, p=0.97) There was also no difference in the risk of these outcomes defined post hoc. Outcome measures and effect size (include 95%CI and p-value if available): CIN1 (=increase in sCr ≥25% over the baseline value in any of the time points: 24, 48 and 120 hours after contrast administration) I: 7 (14%) C: 9 (17%) p>0.05 CIN2 (=increase in sCr	Authors' conclusion Our findings suggest that the addition of NAC does not add further benefit in CIN prevention, compared to standard hydration with isotonic saline infusion.
		5) allergy to iodinate	administration			(=Increase in sCr ≥0.5mg/dL over the	

					1		
		contrast media or NAC				baseline value in any of	
		6) previous enrolment in				the time points: 24, 48	
		the same or other				and 120 hours after	
		protocols				contrast administration)	
		7) administration of				I: 4 (8%)	
		mannitol, theophylline,				C: 5 (9%)	
		dopamine, dobutamine,				p>0.05	
		nonsteroidal anti-				P	
		inflammatory drugs or					
		fenoldopam					
		leneraepani				No acute renal failure	
		N total at baseline:				necessitating renal	
		Intervention: 52				replacement therapy	
		Control: 51				occurred.	
		control. 51				occurred.	
		Important prognostic					
		factors ² :					
		For example					
		age ± SD:					
		l: 71 ± 7					
		C:73 ± 8					
		Sex:					
		I: 94% M					
		C: 84% M					
		C. 04/0101					
		sCr (mg/dL)					
		I: 1.57 ± 0.38					
		C: 1.49 ± 0.30					
		0.1.19 ± 0.30					
		Groups comparable at					
		baseline? Yes					
Ferrario,	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion
2009	randomized	1) patients scheduled for	intervention	(treatment/proced	3 days	effect size (include 95%Cl	
2005	controlled	elective or diagnostic CAG	(treatment/procedu	ure/test):		and p-value if available):	In our experience, NAC
	trial	and/or PCI	re/test):		Loss-to-follow-up:		did not prevent CIN in
		2) age ≥18 years			Intervention:	CIN	patients receiving iso-
		21 age 210 years					patients receiving iso-

Setting:	3) creatinine clearance		Placebo (glucose	4 (4%)	(=increase in sCr	osmolar (iodixanol)
elective	<55ml/min and a stable	NAC 600mg orally	tablets) orally	Reasons not reported	≥0.5mg/dL or >25%	contrast media and
patients,	renal function	every 12 hours for 2	every 12 hours for		within 3 days after the	adequate hydration.
university		days	2 days	Control:	procedure)	
hospital	Exclusion criteria:	(2 doses on the day	(2 doses on the day	4 (3%)	I: 8/99 (8%)	
	1) ongoing acute	before and 2 doses	before and 2 doses	Reasons not reported	C: 6/101 (6%)	
Country: Italy	myocardial infarction or	on the day of	on the day of		P=0.60	
	acute coronary syndrome	contrast	contrast	Incomplete outcome		
Source of	2) renal replacement	administration, total	administration)	<u>data</u> :		
funding: not	therapy	dose 2400mg)		Not reported		
reported	3) allergy to NAC		0.9% saline			
	4) need for administration	0.9% saline	1ml/kg/h in 12-24			
	of mannitol, theophylline,	1ml/kg/h in 12-24	hours before the			
	dopamine, dobutamine,	hours before the	procedure and 24			
	fenoldopam or nephrotoxic	procedure and 24	hours after			
	drugs within 1 week of	hours after				
	procedure					
	5) clinical signs of					
	dehydration and systemic					
	hypotension					
	<u>N total at baseline</u> :					
	Intervention: 99					
	Control: 101					
	Important prognostic					
	factors ² :					
	For example					
	age ± SD:					
	l: 75 ± 8					
	C: 75 ± 7					
	Sex:					
	I: 68% M					
	C: 62% M					
	Creatinine clearance					

		(mL/min) 1: 37 ± 11.5 C: 40 ± 9.3 Groups comparable at baseline? Yes					
Gulel, 2005	Type of study: randomized controlled trial Setting: elective, single centre Country: Turkey Source of funding: not reported	Inclusion criteria: 1) patients scheduled for elective diagnostic CAG 2) chronic renal impairement: sCr >1.3mg/dL 3) stable renal function Exclusion criteria: 1) acute renal failure 2) end-stage renal failure on regular dialysis 3) clinically evident heart failure 4) allergy against contrast agents 5) serious hepatic dysfunction 6) planned PCI <u>N total at baseline</u> : Intervention: 25 Control: 25 <u>Important prognostic</u> factors ² : For example age \pm SD: 1: 61 \pm 12 C: 62 \pm 12	Describe intervention (treatment/procedu re/test): NAC 600mg orally every 12 hours for 2 days (2 doses on the day before and 2 doses on the day of contrast administration, total dose 2400mg) 0.9% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Describe control (treatment/proced ure/test): 0.9% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): Contrast nephropathy (= an increase more than 0.5 mg/dL 48 hours after the procedure compared with baseline values-) l: 3/25 (12%) C: 2/25 (8%) p>0.05	Authors' conclusion: Our results show that oral acetylcysteine does not reduce the risk of contrast nephropathy when used before elective diagnostic CAG in patients with renal dysfunction.

Habib, Type of 2016 randon control trial Setting Europe Gaza Hospita Gaza, Palestii (Israel) Source funding reporte	Iled risk factor for CIN (age >70 years, baseline creatinine level >1.5 mg/dL, heart ievel >1.5 mg/dL, heart failure, diabetes mellitus or contrast media volume >300 mL) al, Exclusion criteria: ne N total at baseline: of Group A: 40 g: not Group C: 40	Describe intervention (treatment/procedu re/test): Group A (n = 30), NAC 1200 mg orally before angiography and 1200 mg orally twice daily for three doses along with good hydration	Describe control (treatment/proced ure/test): Group C (n = 45), hydration with 0.9% saline started just before contrast media injection and continued for 12 h at a rate 1.0 mL/kg/min after angiography or 0.5 mL/kg/h in cases with overt heart failure for 12 h	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%CI and p-value if available): Contrast nephropathy (= an increase more than 0.5 mg/dL 48 hours after the procedure compared with baseline values-) I: 2/30 C: 8/45 P=0.001	Authors' conclusion: Our study indicates that high doses of NAC plus hydration provide better protection against CIN than combination therapy of NAC and ascorbic acid plus hydration, or hydration alone.
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	Groups comparable at baseline? Yes					
Izani Type of study: Wan, randomized 2008 controlled (Mohame d) Setting: elective patients, single centre Country: Malaysia Source of funding: not reported	Inclusion criteria: 1) patients electively admitted for CAG 2) calculated creatinine clearance 40-90ml/min 3) age ≥18 years Exclusion criteria: 1) severe renal failure 2) presence of acute or reversible component of renal failure 3) severe peptic ulcer disease 4) history of allergy to NAC 5) severe asthma 6) pregnancy or breastfeeding N total at baseline: Intervention: 49 Control: 51 Important prognostic factors ² : For example age ± SD: 1: 58 ± 8 C: 56 ± 7 Sex: 1: 86% M C: 82% M	Describe intervention (treatment/procedu re/test): NAC 600mg orally every 12 hours for 2 days (2 doses on the day before and 2 doses on the day of contrast administration, total dose 2400mg) 0.45% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Describe control (treatment/proced ure/test): 0.45% saline 1ml/kg/h in 12 hours before the procedure and 12 hours after	Length of follow-up: 48 hours Loss-to-follow-up: Intervention: 4 (8%) 1 early discharge 2 procedure cancellation 1 procedure complication Control: 4 (7%) 2 early discharge 2 procedure cancellation Incomplete outcome data: As above	Outcome measures and effect size (include 95%CI and p-value if available): CIN (= increase of >25% in the sCr level 48 hours after the procedure) I: 2/49 (4%) C: 6/51 (12%) P=0.27 None of the patients who developed CIN required dialysis.	Authors' conclusion: Addition of NAC to standard hydration therapy is not associated with reduction in incidence of CIN in patients with mild to moderate renal impairment undergoing elective CAG.

Koc, 2012	Type of study: randomized controlled trial Setting: elective patients, single centre Country: Turkey Source of funding: not reported	SCr (μ mol/L) I: 124 ± 17 C: 124 ± 22 Groups comparable at baseline? Yes Inclusion criteria: 1) patients about to undergo CAG and/or PCI 2) calculated creatinine clearance <60ml/min or sCr≥1.1mg/dL 3) age ≥18 years Exclusion criteria: 1) contrast-agent hypersensitivity 2) pregnancy or lactation 3) decompensated heart failure 4) pulmonary edema 5) emergency catheterisation 6) acute or end-stage renal failure N total at baseline: Intervention: 80 Control: 80 Important prognostic factors ² : For example age ± SD:	Describe intervention (treatment/procedu re/test): NAC 600mg intravenously every 12 hours for 2 days (2 doses on the day before and 2 doses on the day of contrast administration, total dose 2400mg) 0.9% saline iv 1ml/kg/h in on the day before, on the day of, and on the day after the procedure	Describe control (treatment/proced ure/test): 0.9% saline iv 1ml/kg/h in on the day before, on the day of, and on the day after the procedure	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN (=baseline sCr ≥25% and/or an absolute increase in sCr of ≥0.5 mg/dL 48 hours after the procedure) I: 2 (3%) C: 13 (16%) P=0.006 No patients needed hemodialysis.	Authors' conclusion: The results of this study suggest that NAC plus high-dose hydration was superior to high-dose hydration alone as well as standard hydration for the protection of renal function in patients with mild to moderate renal dysfunction who are undergoing CAG and/or PCI.

Kotlyar,	Type of study:	Sex: I: 76% M C: 79% M Creatinine clearance (mL/min) I: 59 ± 16 C: 58 ± 16 Groups comparable at baseline? Yes Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Authors' conclusion:
2005	randomised controlled trial Setting: elective patients admitted for 1 day Country: Australia Source of funding:	 day-stay elective patients scheduled for CAG and/or PCI <u>Exclusion criteria</u>: allergy to the study medication unstable renal function undergoing chronic dialysis uncontrolled asthma pregnancy or breastfeeding N total at baseline: 	intervention (treatment/procedu re/test): 11: NAC 300mg intravenously, once 1-2 hours before procedure and once 2-4 hours after procedure (total dose 600mg) Hydration iv: 0.9% saline 100ml/hour 2	(treatment/proced ure/test): Hydration iv: 0.9% saline 100ml/hour 2 hours before procedure and 5hours after procedure	2-4 days and 30 days <u>Loss-to-follow-up</u> : Not reported <u>Incomplete outcome</u> <u>data</u> : Not reported	effect size (include 95%Cl and p-value if available): None of the patients developed CIN (= None of the patients developed a need for dialysis.	For day-saty patients with mild to moderate renal impairement undergoing CAG and/or PCI, prehydration alone is less complicated and more cost-effective than a combination of IV NAC (at doses used) and hydration.
	commercial (pharmaceuti cal company)	In total at baseline.11: 2012: 21C: 19Important prognostic $factors^2$:For example $age \pm SD$:11: 66 \pm 1412: 67 \pm 12	hours before procedure and 5hours after procedure 11: NAC6300mg intravenously, once 1-2 hours before				

		C: 69 ± 9 Sex: 11: 75% M 12: 86% M C: 89% M SCR (mmol/L) 11: 0.16 \pm 0.03 12: 0.16 \pm 0.03 C: 0.15 \pm 0.02 Groups comparable at baseline? Yes	procedure and once 2-4 hours after procedure (total dose 1200mg) Hydration iv: 0.9% saline 100ml/hour 2 hours before procedure and Shours after procedure				
Sadineni, 2017	Type of study: randomized controlled trial Setting: Department of Nephrology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India Source of funding: not reported	Inclusion criteria: Age more than 30 years + Patients should have their serum creatinine ≥1.2 mg/dl on their most recent sample drawn within 3 months of planned procedure Exclusion criteria: Patients with acute renal failure, endstage renal disease requiring dialysis, intravascular administration of contrast material within previous 6 days, pregnancy, lactation, emergent coronary angiography, history of hypersensitivity reaction to contrast media, cardiogenic shock, pulmonary edema,	Describe intervention (treatment/procedu re/test): NAC + NS: Group of patients who received NS and NAC	Describe control (treatment/proced ure/test): Placebo + NS: Group of patients who received NS only	Length of follow-up: 48 hours Loss-to-follow-up: Not reported Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): CIN, defined as either a relative increase in serum creatinine from baseline of ≥25% or an absolute increase of ≥0.3 mg/dl (44.2 µmol/L) during days 1 and 2 NAC: 7/35 Placebo: 11/30 P > 0.05	Authors' conclusion: The major finding of this study was there was no significant difference between NAC and placebo in the prevention of contrast nephropathy.

mechanical ventilator, parenteral use of diuretics,	
parenteral use of diuretics,	
recent use of NAC, recent	
use of ascorbic acid, and	
use of metformin or	
NSAIDS within 48 h of	
procedure were excluded	
from the study.	
N total at baseline:	
NAC: 35	
Placebo: 30	
Important prognostic	
factors ² :	
For example	
age ± SD:	
NAC: 61 ± 11	
Placebo: 63 ± 12	
Sex:	
Group A: 77% M	
Group C: 87% M	
Groups comparable at	
baseline? Yes	
Seyon, Type of study: Inclusion criteria: Describe Describe control Length of follow-up: Outcome measures and	Authors' conclusion
2007 randomized 1) patients admitted with a intervention (treatment/proced 48 hours effect size (include 95%	СІ
controlled diagnosis of acute coronary (treatment/procedu ure/test): and p-value if available	: These results suggest
trial syndrome re/test): Loss-to-follow-up:	that this cohort gained no
2) scheduled for CAG Iv hydration 0.45% Not reported CIN	added protection to renal
Setting: and/or PCI 600mg NAC orally saline1ml/kg/hour (=increase in sCr	function with the use of
emergency 3) impaired renal function four doses in total 4-6 hours before Incomplete outcome >44µmol/L (0.5mg/dL)	NAC
patients, one defined as: (1 before procedure and 12 hours after data: and/or 25% above	
centre -calculated creatinine and 3 after every 12 procedure Not reported baseline within 48 hour	s)
clearance <50ml/min or hours) I: 1/20 (5%)	
Country: $-sCr \ge 1.4 mg/dL$ for males or C: 2/20 (10%)	

4) age 218 years a line1.m1/kg/hour Source of Exclusion criteria: 1) hemodynamic instability and 12 hours after reported 3 acute gastrointestinal 3 acute gastrointestinal dialysis therapy. 3) acute gastrointestinal disorder 4) No patients required dialysis therapy. 9) acute gastrointestinal disorder 4) NYHA III or IV, or patients deemed by cardiologist usuitable for V hydration sperimental drugs 8) participation in another study or use of study or use of for komple Intervention: 20 Control: 20 Important prognostic for example get s5D: i.7.6.5 i.7.75.5 0 Sex: i. 60% M c. 70% M	r						
Source of reported 4-6 hours before and 12 hours after procedure reported 1) hemodynamic instability requiring inotropic support 1) programs add 12 hours after procedure 1) programs add 12 hours after procedure 1) production of the support add 12 hours after procedure 1) production of the support add 12 hours after procedure 1) function of the support add 12 hours after procedure 1) Killip class III or IV or Night ass III or IV or Night ass III or IV or available for iv hydration sight asset as a support of the support is a support to the support is a support of the support is a support is a support of the support is a s	Car	inada	sCr≥1.3mg/dL for females	Iv hydration 0.45%		p<0.05	
funding: not reportedExclusion criteria: 1) hemodynamic instability 2) pregnancy 3) acute gastrointestinal disorder 4) Killip class II or IV or NYHA II or IV, or patients deemed by cardiologist unsuitable for iv hydration 5) known sensitivity to NAC 6) current treatment with theophylline or manited 7) dialysis therapy.No patients required dialysis therapy.No patients required disorderNo patients required dialysis therapy.No patients required dialysis therapy.No patients required disorderNo patients required dialysis therapy.No patients required dialysis therapy.No patients required disorderNo patients required dialysis therapy.No patients required to ny constant devicesNo patients required dialysis therapy.No patients required to ny constant devicesNo patients required dialysis therapy.No patients required to ny constant devicesNo patients required to ny constant devicesNo patients required to ny constant devicesNo patients required disorderNo patients required to ny constant devicesNo pat			4) age ≥18 years	saline1ml/kg/hour			
reported 1) hemodynamic instability requiring instropic support procedure dialysis therapy. 2) pregnancy 3) acute gastrointestinal disorder 4) Killy class III or IV or NYHA III or IV, or patients hemodynamic Instability deemed by cardiologist unsutable for iv hydration 6) current treatment with theophylline or manitol 7) dialysis therapy hemodynamic Instability 1) dialysis therapy hemodynamic Instability 1) dialysis therapy Nitoria at baseline: Intervention: 20 Control: 20 Nitoria these intervention: 20 Control: 20 hemodynamic Instability 176 ± 6 Cr 75 ± 10 hemodynamic Instability 176 ± 6 Cr 75 ± 10 Sev: I: 60% M C: 70% M Sev: I: 60% M C: 70% M hemodynamic Instability 100 ± 100 hemodynamic Instability 100 ± 100	So	urce of		4-6 hours before			
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2) pregnancy 3) acute gastrointestinal disorder 4) Killip class II or IV or NYHA III or IV, or patients deemed by cardiologist unsuitable for iv hydration 5) known sensitivity to NAC 6) current treatment with theophylline or manitol 7) dialysis therapy 8) participation in another study or use of experimental drugs N total at baseling: Intervention: 20 Control: 20 Important prognostic factors ¹ : For example age ± 50: 1: 76 ± 6 C: 75 ± 10 Sex: 1: 60% M C: 70% M				•			
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I: 60% M C: 70% M							
I: 60% M C: 70% M			Sex:				
C: 70% M							
Groups comparable at							
			Groups comparable at				

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Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

CAG: coronary angiography; CECT: contrast-enhanced computed tomography; CI: confidence interval; CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; iv: intravenous; NAC: N-acetylcysteine; NYHA: New York Heart Association; OR: odds ratio; PCI: percutaneous coronary intervention; SCr: serum creatinine

Search des	cription	
Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. (111910)	302
(OVID)	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
2005-juli	(535114)	
2015	3 1 and 2 (8902) 4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
English	ciaki).ti,ab. (1951) 5 3 or 4 (9390)	
	6 limit 5 to (yr="2005 -Current" and (dutch or english)) (3922)	
	7 Acetylcysteine/ or ('acetyl cysteine' or acetylcysteine or (n adj1 acetyl*)).ti,ab. (71339)	
	8 6 and 7 (356)	
	9 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic*	
	or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab.	
	or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection	
	criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (245460)	
	10 8 and 9 (50) – 49 uniek	
	11 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind	
	Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or	
	clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or	
	random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj	
	(blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1499747)	
	12 8 and 11 (184)	
	13 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or	
	studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or	
	(observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or	
	prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies	
	vallen ook longitudinale, prospectieve en retrospectieve studies] (2196775)	
	14 8 and 13 (107) 15 12 not 10 (144) – 141 uniek	
	16 14 not (10 or 12) (23)	
Embase	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2	
(Elsevier)	(nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3	
	medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2	
	(disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)) NOT 'conference	
	abstract':it AND [english]/lim AND [embase]/lim AND [2005-2015]/py	
	AND ('acetylcysteine'/exp/mj OR 'acetyl cysteine':ab,ti OR acetylcysteine:ab,ti OR (n NEAR/1 acetyl*):ab,ti)	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR	
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR	
	'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR	
	'nonhuman'/exp NOT 'human'/exp))) (70) – 21 uniek	
	AND 'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR	
	'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR	
	'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR	
	placebo*:ab,ti NOT 'conference abstract':it)) (171) – 56 uniek	
	AND 'major clinical study'/de (25) – 12 uniek	

Evidence tables

Table: Exclusion after revision of full text

Author and year	Reason for exclusion
Albabtain, 2013	Included in systematic review by Sadat, 2013
Alexopoulos, 2010	No vitamin C administration in one of the treatment groups
Au, 2014	review, not specifically focussed on vitamin C (review of Sadat, 2013 of better
	quality and includes same literature)
Boscheri, 2005	Included in systematic review by Sadat, 2013
Briguori, 2006	review, not systematic
Briguori, 2007_1	vitamin C group not being compared to hydration only or no hydration group (does
	not comply with PICO)
Briguori, 2007_2	vitamin C group not being compared to hydration only or no hydration group (does
	not comply with PICO)
Bruerck, 2013	Included in systematic review by Sadat, 2013
De Bie, 2011	review, not systematic
Generali, 2012	review, not systematic
Itoh, 2005	review, not systematic
Jo, 2009	Included in systematic review by Sadat, 2013
Joannidis, 2007	review, not systematic
Kayan, 2012	Not a clinical study
McCullough, 2008	Letter to editor
McCullough, 2013	Letter to editor
Naziroglu, 2013	review, not specifically focussed on vitamin C (review of Sadat, 2013 of better
	quality and includes same literature)
Oudemans – van Straaten,	review, not systematic
2005	
Pattharanitima, 2014	review, not systematic
Reiner, 2009	review, not systematic
Sadat, 2015	review, not systematic
Shakeryan, 2013	oral administration of vitamin C in combination with pentoxyfilline in treatment
Sin aut. 2007	group (does not comply with PICO)
Sinert, 2007 Sinert, 2013	more recent review by Sadat, 2013 available review, not systematic
	Included in systematic review by Sadat, 2013
Spargias, 2005	
Stacul, 2006	more recent review by Sadat, 2013 available Article not found
Wang, 2014	
Zhou, 2012	Included in systematic review by Sadat, 2013

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10;doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097;

doi:10.1371/journal.pmed1000097)

Study First	Appropriate and clearly focused question? ¹	Comprehensive and systematic literature search? ²	Description of included and excluded studies? ³	Description of relevant characteristics of included studies? ⁴	Appropriate adjustment for potential confounders in observational studies? ⁵	Assessment of scientific quality of included studies? ⁶	Enough similarities between studies to make combining them reasonable? ⁷	Potential risk of publication bias taken into account? ⁸	Potential conflicts of interest reported? ⁹
author, year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Sadat, 2013	Yes	Yes	No	Yes	Not applicable	Yes	Yes	Yes	Yes

1. Research question (PICO) and inclusion criteria should be appropriate and predefined

2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched

3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons

4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported

5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)

6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)

7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?

8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)

Research question:

Study reference (first author,	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ²	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴	Bias due to loss to follow-up? ⁵	Bias due to violation of intention to treat analysis? ⁶
publicatio n year)		(unlikely/likely/un clear)	(unlikely/likely/un clear)	(unlikely/likely/un clear)	(unlikely/likely/uncle ar)	(unlikely/likely/unc lear)	(unlikely/likely/uncle ar)	(unlikely/likely/uncle ar)
Komiyama 2017	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear
Dvoršak, 2013	Not reported	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

- 3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
- 4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
- 5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
- 6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for systematic review of RCTs and observational studies (intervention studies) Research question:

Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments
reference	characteristics			control (C)		effect size	
Sadat,	SR and meta-	Inclusion criteria SR:	Describe intervention:	Describe control:	End-point of	Outcome measure-1	Facultative:
2013	analysis of	 RCTs assessing the use of 			follow-up:	Defined as. Risk of CI-AKI	
	[RCTs]	ascorbic acid in reducing CI-		A: placebo with IV	Not reported	(risk ratio)	Brief description of
[individua		AKI compared with placebo	A: Ascorbic acid, oral	hydration as in			author's conclusion:
l study	Literature search	or other pharmacological	administration,	ascorbic acid arm		Effect measure: relative	Ascorbic acid provides
characteri	up to May 15 th	treatments in patients	3g at least 2 hours after	B: placebo with IV	For how many	risk [95% CI]:	effective
stics	2013	undergoing coronary	procedure, 2g night	hydration as in	participants	A : 0.46 (0.23 – 0.90)	nephroprotection against
deduced		angiography	before and morning	ascorbic acid arm	were no	B : 1.55 (0.39 – 6.26)	CI-AKI and may form a
from [1st	A: Sparglas,	route of administration of	after procedure.	C : 1200mG NAC	<u>complete</u>	C : 3.65 (0.42 – 31.99)	part of effective
author,	2004	ascorbic acid: oral or	Hydration with saline	orally 2x/daily on	outcome data	D : 1.35 (0.40 – 4.61)	prophylactic
year of	B: Boscheri,	intravenous or both	50-125mg/hr IV from	day of procedure	available?	E : 0.25 (0.08 – 0.81)	pharmacological
publicatio	2007	3) Incidence of CI-AKI	time of randomization	and day before	(intervention/co	F : 0.76 (0.51 – 1.14)	regiments.
n	C : Jo, 2009	(absolute increase in serum	to at least 6 hours after	procedure	ntrol)	G : 1.14 (0.32 – 4.07)	
]]	D : Zhou, 2011	creatinine of ≥0.5 mg/dl	procedure	D: IV saline	Not reported	H : 0.46 (0.32 – 2.30)	Personal remarks on
	E: Komiyama,	(44µmol/L) or a relative	B: 1g ascorbic acid	hydration		I: 0.49 (0.09 – 2.30)	study quality,
PS., study	2011	increase of ≥25% from the	orally 20 minutes before	1mg/kg/hour for 4			conclusions, and other
characteri	F: Bruerck, 2011	baseline value after	exposure to contrast	hours before and at		Pooled effect (random	issues (potentially)
stics and	G : Li, 2012	administration of contrast	medium, 500mL saline,	least 12 hours after		effects model): risk ratio:	relevant to the research
results	H: Albabtain,	media during angiography)	2 hours before and	angiography		0.672 [95% CI 0.466 to	question:
are	2013	was reported as outcome	500ml during	E: IV saline		0.969] favoring ascorbic	
extracted	I:Hamdi, 2013	measure	angiography and	hydration 1.5 – 2.5L		acid	When studies on oral
from the			subsequent 6 hours	F: placebo (per		Heterogeneity (I ²): 27%	ascorbic acid
SR (unless	Study design:	Exclusion criteria SR:	C: ascorbic acid, 3g	ascorbic acid dose)			administration and IV
stated	RCT [parallel]	-	(night before) and 2g	and IV saline		Outcome measure-2	ascorbic acid
otherwise			morning of procedure;	(1/mg/kg/hour) for		Risk of publication bias	administration were
)	Setting and	9 studies included	2g night before and	12 hours before to		Egger's regression	pooled separately, the
	Country:		morning after	12 hours after		intercept:	ascorbic acid
	Outpatients		procedure, oral	contrast medium		1.086 (95% CI: -2.57 –	administration was as
	England and	Important patient	administration, all doses	exposure		4.74)	effective as control in
	Pakistan	characteristics at baseline:	12 hours apart	G: IV saline		df = 4	prevention of CI-AKI.
		Number of patients;	D: ascorbic acid, IV	hydration		p=0.455	
	Source of	characteristics important to	administration, 3g	H: IV saline			Level of evidence: GRADE
	<u>funding:</u>	the research question and/or	morning of procedure,	hydration			(per comparison and

Not reported	for statistical adjustment	oral 0.5g on the night of	I:IV saline hydration		outcome measure)
	(confounding in cohort	procedure and next	,		including reasons for
	studies); for example, age,	morning (all doses 12			down/upgrading:
	sex, bmi,	hours apart). IV saline			For the outcome risk of
		hydration1mg/kg/hr for			CI-AKI the level of
	<u>N,</u>	4 hours before and at			evidence was reduced to
	<u>N,</u> A : 238	least 12 hours after			moderate, due to
	B : 143	angiography			inconsistency of results.
	C : 212	E: ascorbic acid, IV			
	D : 174	administration, 3g			
	E : 70	before procedure, 2g			
	F : 520	night and morning after			
	G : 149	procedure (12 hours			
	H : 243	apart). Saline hydration			
	I:202	1.5 – 2.5L			
		F: ascorbic acid, IV			
		administration			
	Groups comparable at	G: ascorbic acid, IV 3g 2-			
	baseline?	4 hours before			
	Unclear	procedure and oral 1g			
		on days 1 and 2 after			
		procedure. IV saline			
		hydration			
		H: ascorbic acide, oral			
		administration, 3g 2			
		hours before procedure,			
		2g after angiogram and			
		2g 24 hours after			
		angiogram. IV saline 50-			
		125 ml/hour from			
		randomization until at			
		least 6 hours after			
		procedure			
		I: ascorbic acid 3g 2			
		hours before procedure,			
		2g day after procedure			
		and next day, mode of			

	administration not		
	reported		

Ascorbic acid = vitamin C;CI-AKI: contrast-induced acute kidney injury; CIN: contrast induced nephropathy; IV: intravenous; NAC: N-acetyl-cysteine; NR: not reported; RCT: randomised controlled trial

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1 This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study reference	Study characteristic s	Patient characteristics ²	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
Dvoršak, 2013	Type of study: randomized controlled trial Setting: not clear Country: Slovenia Source of funding: no funding	Inclusion criteria: 1) patients with stable serum creatinine levels (>107µmol/L / 1.2 mg/dL) 2) undergoing elective coronary angiography or angioplasty Exclusion criteria: 1) regular medication containing vitamin C 2) acute renal failure 3) end-stage renal disease 4) radiocontrast procedure in the last 3 months 5) cardiogenic shock 6) acute myocardial infarction <u>N total at baseline</u> : Intervention: 42 Control: 41	Describe intervention (treatment/procedu re/test): Ascorbic acid in 500mg capsules 3g orally before procedure 2g after the procedure in the evening and the next morning	Describe control (treatment/proced ure/test): Placebo	Length of follow-up: 4 days Loss-to-follow-up: Intervention: 2/42 (5%) Reasons: lost to follow-up (?) Control: 0/41 (0%) Reasons: not applicable Incomplete outcome data: Not reported	Outcome measures and effect size (include 95%Cl and p-value if available): Contrast-induced nephropathy (+an increase in serum creatinine level >25% from baseline or increase of serum cystatin C levels >25%, measured 3-4 days after procedure) I: 2/40 C: 3/41 P=0.51	We found no statistically significant impact of ascorbic acid on the incidence of CIN in patients with chronic renal impairment undergoing coronary arteriography or angioplasty.
		Important prognostic					

		factors ² :					
		For example					
		age ± SD:					
		I: 71 ± 9					
		C: 71 ± 9					
		Sex:					
		I: 78% M					
		C: 68% M					
		Groups comparable at					
		baseline? Yes					
Komiyam	Type of study:	Inclusion criteria:	Describe	Describe control	Length of follow-up:	Outcome measures and	Use of i.v. sodium
a 2017	randomized	patients with renal	intervention	(treatment/proced	<u>3 days</u>	effect size (include 95%Cl	bicarbonate and ascorbic
	controlled	dysfunction undergoing	(treatment/procedu	ure/test):		and p-value if available):	acid and a saline
	trial	elective angiography	re/test):		Loss-to-follow-up:		hydration protocol in
		(including coronary			Intervention:	Contrast-induced	patients with CKD
	Setting:	angiography, aortography,	Sodium bicarbonate	The control group	None reported	nephropathy	undergoing elective
	hospital	and venography)	(20 mL=20 mEq;	received 0.9%	<u>Reasons: not applicable</u>	(+an increase in serum	procedures can prevent
		or intervention (including	Meyron 84, Otsuka	physiological saline		creatinine level >25%	CIN more effectively than
	Country:	percutaneous coronary	Pharmaceutical,	6–15 h before, and	<u>Control:</u>	from baseline or increase	saline hydration alone.
	Japan	intervention and	Tokyo, Japan) and	during, the	None reported	of serum cystatin C levels	
		<u>endovascular treatment)</u>	ascorbic acid (3 g)	procedure at a rate	<u>Reasons: not applicable</u>	>25%, measured 3 days	
	Source of	with a catheter	were given i.v.	of 1.5 mL/kg/h.		after procedure)	
	funding: no		before the	This rate was then	Incomplete outcome		
	funding	Exclusion criteria:	procedure. Ascorbic	increased to 2.5	<u>data:</u>	I: 6/211	
		<u>1) aged <20 years</u>	acid (2 g) was then	mL/kg/h for 6 h	Not reported	C: 19/218	
		pregnant or undergoing	administered after	after the		P=0.008	
		<u>maintenance dialysis. 3)</u>	the procedure,	procedure. The			
		acute conditions such as	followed by another	total amount of			
		acute myocardial infarction	2 g of ascorbic	saline administered			
		and unstable angina	acid 12 h later after	was 1,500–2,500			
		3) severe cardiac failure	the procedure; this	mL			
		<u>(New York Heart</u>	group also received				
		Association class III or	the same saline				
		<u>higher)</u>	hydration protocol				
		4) severe respiratory	as the control				

	<u>disease</u>	group.		
	5) undergone catheter			
	procedures involving the			
	use of a contrast agent			
	within the previous 48 h			
	N total at baseline:			
	Intervention: 218			
	Control: 211			
	Important prognostic			
	factors2:			
	For example			
	age ± SD:			
	l: 73 ± 10			
	<u>C: 74 ± 10</u>			
	Sex:			
	I: 79% M			
	<u>C: 82% M</u>			
	Groups comparable at			
	baseline? Yes			
Neter				

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	113
(OVID)	(110542) 2 over Kidney Diseases (or (((kidney or repeal) adi2 (diseases* or injur* or failure*)) or	
1005 :	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
1995-june	(528935) 3 1 and 2 (8818)	
English, Dutch	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or ciaki).ti,ab. (1925)	
	5 3 or 4 (9301) 6 limit 5 to (yr="1995 -Current" and (dutch or english)) (5402) 9 "Ascorbic Acid"/ (36223)	
	10 ("vitamine C" or ascorbate or "ascorbic acid*").ti,ab. (36094) 11 9 or 10 (52727) 12 6 and 11 (32)	
	14 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (241238)	
	15 12 and 14 (8) – 7 uniek 16 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) (1475337)	
	 (14/3537) 17 12 and 16 (19) 18 Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or Cohort analy\$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective.tw. or prospective.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] (2167237) 19 12 and 18 (8) 20 15 or 17 or 19 (21) 21 17 or 19 (19) not 15 (13) 	
Embase (Elsevier)	¹²¹ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹⁷ ¹	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT (animal* NOT human*) – 31 – 27 uniek	
	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti OR 'clinical study'/exp) – 79 – 66 uniek	

Appendix 1 Additional meta-analyses

Figure 7.9 Meta-analysis also including the studies published in abstract form only

Study or Subgroup 🛆		vitamin C plus		hydration		Risk Ratio	Risk Ratio
		Total	Events Total		Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Albabtain 2013	2	57	5	66	4.4%	0.46 [0.09, 2.30]	
Boscheri 2007	5	74	3	69	5.7%	1.55 [0.39, 6.26]	
Brueck 2011	24	98	62	193	43.1%	0.76 [0.51, 1.14]	
Dvorsak 2013	2	40	3	41	3.8%	0.68 [0.12, 3.88]	
Komiyama 2011	5	78	4	71	6.8%	1.14 [0.32, 4.07]	
Li 2012	3	35	12	35	7.9%	0.25 [0.08, 0.81]	
Spargias 2004	11	118	23	113	21.0%	0.46 [0.23, 0.90]	
Zhou 2011	6	82	4	74	7.3%	1.35 [0.40, 4.61]	
Total (95% CI)		582		662	100.0%	0.68 [0.48, 0.96]	\bullet
Total events	58		116				
Heterogeneity: Tau ² = 0.03; Chi ² = 7.85, df = 7 (P = 0.35); I ² = 11%							
Test for overall effect: Z = 2.19 (P = 0.03)							0.01 0.1 1 10 100 Favours vitamin C Favours placebo

Figure 7.10 Meta-analysis including all RCTs on vitamin C (both impaired kidney function and kidney function not reported)

Chudu as Cubasaua	ascorb	ic acid	plac	ebo	Weight	Risk Ratio M-H, Random, 95% CI	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight		M-H, Random, 95% CI
Spargias 2004	11	118	23	113	17.1%	0.46 [0.23, 0.90]	
Boscher 2007	5	74	3	69	4.4%	1.55 [0.39, 6.26]	
Zhou 2011	6	82	4	74	5.6%	1.35 [0.40, 4.61]	
Komiyama 2011	3	35	12	35	6.1%	0.25 [0.08, 0.81]	
Li 2012	5	78	4	71	5.2%	1.14 [0.32, 4.07]	
Albabtain 2013	2	57	5	66	3.4%	0.46 [0.09, 2.30]	
Dvorsak 2013	2	40	3	41	2.9%	0.68 [0.12, 3.88]	
Hamdi 2013	11	107	20	95	16.6%	0.49 [0.25, 0.97]	
Bruerck 2013	24	98	62	193	38.6%	0.76 [0.51, 1.14]	
Total (95% CI)		689		757	100.0%	0.65 [0.48, 0.87]	•
Total events	69		136				2002
Heterogeneity: Tau ² = 0.02; Chi ² = 8.67, df = 8 (P = 0.37); l ² = 8%							
Test for overall effect: Z = 2.88 (P = 0.004)							0.1 1 10 10 Favours ascorbic acid Favours placebo

-	r examination of full text
Author and year	Reasons for exclusion
Aspelin, 2014	Exam questions, not an original article
Baris, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Cirit, 2006	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Del Veccio	Narrative review
Diogo, 2010	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Duan, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
0	injury)
Goo, 2014	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
0	radiological examination with intravasal contrast)
Gu, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
C 2015	injury)
Gu, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney injury)
Jo, 2015	Only abstract available (full tekst nogmaals aangevraagd bij Sanne, aan de hand hiervan
JU, 2015	alsnog inclusie mogelijk)
Kalyesubula, 2014	Narrative review
Kalyesubula, 2014 Kellum, 2001	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
Kellulli, 2001	radiological examination with intravasal contrast)
Kiski, 2010	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
RISKI, 2010	radiological examination with intravasal contrast)
Lapi, 2014	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
Lapi, 2014	radiological examination with intravasal contrast)
Li, 2011	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination with intravasal contrast)
Li, 2012	Narrative review
Li, 2012b	Only abstract available (full tekst nogmaals aangevraagd bij Sanne, aan de hand hiervan
	alsnog inclusie mogelijk)
Marenzi, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Mauer, 2002	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Oguzhan, 2013	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
0,	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Onuigbo, 2008	No control group
Onuigbo, 2009	Narrative review
Onuigbo, 2012	Narrative review
Onuigbo, 2015	Editorial comment, not an original article
Patel, 2011	Narrative review
Peng, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Rim, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to
	radiological examination but started, with the hypothesis that this will prevent kidney
	injury)
Rim, 2013	Erratum of Rim, 2012; not an original article
Ryan, 2008	Narrative review

Saudan, 2008	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination but started, with the hypothesis that this will prevent kidney injury)
Schetz, 2004	Narrative review
Shehata, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Shemirani, 2012	Patients with normal kidney function
Spatz, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Umruddin, 2012	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Wolak, 2013	Patients with normal kidney function
Wu, 2015	Does not fulfill selection criteria (nephrotoxic medication is not stopped prior to radiological examination with intravasal contrast)
Zhou, 2013	Narrative review

Risk of bias table for intervention studies (randomized controlled trials)
Research question:

Study reference (first author, publicatio n year)	Describe method of randomisation ¹	Bias due to inadequate concealment of allocation? ² (unlikely/likely/un	Bias due to inadequate blinding of participants to treatment allocation? ³	Bias due to inadequate blinding of care providers to treatment allocation? ³	Bias due to inadequate blinding of outcome assessors to treatment allocation? ³	Bias due to selective outcome reporting on basis of the results? ⁴ (unlikely/likely/uncle	Bias due to loss to follow-up? ⁵ (unlikely/likely/uncle ar)	Bias due to violation of intention to treat analysis? ⁶ (unlikely/likely/unclea
ii year)		clear)	(unlikely/likely/un clear)	(unlikely/likely/un clear)	(unlikely/likely/uncl ear)	ar)	ai)	r)
Bainey, 2015	Permuted block- randomization; computerized intractive voice- response system	Unlikely	Unlikelu	Unclear	Unclear	Unlikely	Unclear	Unlikely
Rosenstoc k, 2008	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

1. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

2. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

3. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

4. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

5. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

6. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])1 This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study	Study	Patient	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome	Comments
reference	characteristics	characteristics ²				measures and	
Bainey, 2015	Type of study: Randomized controlled trial (pilot) Setting: outpatients and inpatients Country: Canada Source of funding: both commercial and non- commercial	Inclusion criteria:1) presented forcardiaccatheterization2) using an ACEi orARB3) moderatechronic kidneydisease (≥ 1.7 mg/dL within 3months or ≥ 1.5 within one weekof cardiaccatheterisation)Exclusion criteria:1) end-stage renaldisease2) emergencycardiaccatheterisationwith insufficienttime to hold ACEi3) pulmonaryoedemaN total at baseline:208Intervention: 106	Describe intervention (treatment/procedure/test): Angiotensin II blockade medication was stopped at least 24 hours prior to catheterisation and restarted after up to 96 hours after. Intravenous normal saline at 3 mL/kg/hour for at least an hour before contrast injection, intravebous normal saline at 1 mL/kg/hour during contrast exposure and 6 hours after the procedure or until discharge.	Describe control (treatment/procedure/test): No discontinuation of angiotensin II blockade medication Intravenous normal saline at 3 mL/kg/hour for at least an hour before contrast injection, intravebous normal saline at 1 mL/kg/hour during contrast exposure and 6 hours after the procedure or until discharge.	Length of follow-up: 72±24 hours	effect size ⁴ Outcome measures and effect size (include 95%Cl and p-value if available): Mean serum creatinine change I: 0.1 ± 0.3 C: 0.3 ± 0.5 P=0.03 Contrast induced AKI: I: 10.9% C: 18.4% HR: $0.59, 95\%$ CI: 0.30 - 1.19, p=0.16 Mortality: I: $0(0\%)$ C: $1(1\%)$ Ischemic stroke: I: $0(0\%)$ C: $1(1\%)$ Rehospitalization	Contrast induced AKI defined as an absolute rize in serum creatinine of ≥25% (44µmol/L) from baseline and/or a relative rise of serum creatinine of ≥25% compared with baseline at any time between 48 and 96 hours post procedure.

		Control: 102 <u>Important</u> <u>prognostic</u> <u>factors²</u> : For example age ± SD: 1: 73 ± 9 C: 72 ± 8 Sex: 1: 74% M C: 73 % M Groups				for cardiovascular cause: l: 0 (0%) C: 3 (2%)	
		comparable at baseline? yes					
Rosenstock,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome	Measurements of
2008	Randomized	1) patients	(treatment/procedure/test):	(treatment/procedure/test):	follow-up: 24	measures and	creatinine 24 hours
	controlled trial	undergoing		1) No Discontinuation of ACT	hours	effect size (include	post-procedure;
	Setting: unclear	coronary angiography		 No Discontinuation of ACE inhibitor use around coronary 		95%Cl and p-value if available):	various ACE-inhibitor subgroups not
	Setting, uncied	2) chronic use (>2	Discontinuation of ACE inhibitor	angiography	Loss-to-	Incidence of CIN	compared due to
	Country:	months) of ACE-	use		follow-up:		small sample size.
	unclear	inhibitor	Morning of procedure up to 24	2) ACE-inhibitor naïve patients	unclear	ACE-inhibitors	
			hours after coronary angiography	undergoing coronary angiography		discontinued:	
	Source of	Exclusion criteria:			Intervention:	3.7%	
	funding: unclear	unclear	Patients were hydrated based on the institution's policies and	Patients were hydrated based on the institution's policies and	N (%) Reasons	ACE-inhibitors not discontinued:	
	unclear	N total at baseline:	medications such as diuretics and	medications such as diuretics and	(describe)	6.2%	
		Intervention: 107	metformin were held prior to	metformin were held prior to	(2000)	ACE-inhibitor	
		Control: 113	procedure	procedure	Control:	naïve group: 6.3%	
		ACE-naïve			N (%)	P=0.66	
		patients: 68			Reasons		
		Important			(describe)		
		Important prognostic			Incomplete		
		prognostic		l	meompiete	1	

1st author, year of publication	Type of study: Setting: Country: Source of funding:	factors ² : unclear For example age ± SD: l: C: Sex: l:% M C:% M Groups comparable at baseline? Incidence of diabetes and hypertension was significantly lower in the ACE-naïve group Inclusion criteria: Exclusion criteria: N total at baseline: Intervention: Control: Important	Describe intervention (treatment/procedure/test):	Describe control (treatment/procedure/test):	Outcome data: unclear Intervention: N (%) Reasons (describe) Control: N (%) Reasons (describe) Length of follow-up: Intervention: N (%) Reasons	Outcome measures and effect size (include 95%Cl and p-value if available):	
	Source of	Intervention: Control: Important			<u>follow-up</u> : Intervention: N (%) Reasons		
		prognostic <u>factors²</u> : For example age ± SD: I: C:			(describe) Control: N (%) Reasons (describe)		
		Sex: I: % M			Incomplete outcome		

		С: % М			data:		
					Intervention:		
		Groups			N (%)		
		comparable at			Reasons		
		baseline?			(describe)		
					. ,		
					Control:		
					N (%)		
					Reasons		
					(describe)		
1st author,	Type of study:	Inclusion criteria:	Describe intervention	Describe control	Length of	Outcome	
year of			(treatment/procedure/test):	(treatment/procedure/test):	follow-up:	measures and	
publication	Setting:	Exclusion criteria:				effect size (include	
-	_					95%CI and p-value	
	Country:	N total at baseline:			Loss-to-	if available):	
	-	Intervention:			follow-up:		
	Source of	Control:			Intervention:		
	funding:				N (%)		
		Important			Reasons		
		prognostic			(describe)		
		factors ² :					
		For example			Control:		
		age ± SD:			N (%)		
		<i>I:</i>			Reasons		
		С:			(describe)		
		Sex:			Incomplete		
		I: % M			outcome		
		С: % М			<u>data</u> :		
					Intervention:		
		Groups			N (%)		
		comparable at			Reasons		
		baseline?			(describe)		
					Control:		
					N (%)		
					Reasons		

					(describe)	
-	A-1	• •		 		

ACEi: angiotensin converting enzyme inhibitor; AKI: acute kidney injury; ARB: angiotensin receptor blocker; CIN: contrast induced nephropathy; HR: hazard ratio

Notes:

- 1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
- 2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
- 3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
- 4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search terms

Database	Search terms	Tota
Parangse	 Jexp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. (112523) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab. (537836) 3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9122) 4 1 and 2 (8979) 10 3 or 4 (16547) 12 exp "Angiotensin Receptor Antagonists"/ (18363) 13 exp Angiotensin-Converting Enzyme Inhibitors/ (40094) 14 exp Diuretics/ (72995) 15 exp Anti-Inflammatory Agents, Non-Steroidal/ (164802) 16 12 or 13 or 14 or 15 (279958) 17 ((Angiotensin* adj3 (Antagonist or Inhibitor* or blocker*)) or Diuretic* or "Non-Steroidal Anti-Inflammatory Agent*" or NSAID* or (nephrotoxic adj3 medic*)).ti,ab. (74424) 18 12 or 13 or 14 or 15 or 17 (307695) 19 10 and 18 (641) 20 limit 19 to (yr="2000 -Current" and (dutch or english)) (266) 21 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or esp. Review Literature as Topic") or contrane.ab. or contrane.jw. or embase.ab. or medine.ab. or (psychilt or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (249387) 22 20 and 21 (26) - 25 uniek 23 (exp clinical trial, phase i or controlled trial or randomized controlled trial or randomized controlled trial, phase ii or clinical trial, phase iii or clinical trial, phase iii or clinical trial, phase ii or controlled clinical trial, phase io r controlled trial or andomized controlled trial o	320
	27 24 or 26 (128) 28 27 not 22 (109) – 107 uniek 'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti))	
	AND ('angiotensin receptor antagonist'/exp/mj OR 'dipeptidyl carboxypeptidase inhibitor'/exp/mj OR 'diuretic agent'/exp/mj OR 'nonsteroid antiinflammatory agent'/exp/mj OR (angiotensin* NEAR/3 (antagonist OR inhibitor* OR blocker*)):ab,ti OR diuretic*:ab,ti OR 'non-steroidal anti-inflammatory agent':ab,ti OR 'non-steroidal anti-inflammatory agents':ab,ti OR nsaids:ab,ti OR (nephrotoxic NEAR/3 medic*):ab,ti)	
	AND ([dutch]/lim OR [english]/lim) AND [embase]/lim AND [2000-2015]/py	
	'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp)) (38) – 26 uniek	
	'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it	
	OR 'clinical study'/exp NOT 'conference abstract':it (225) – 162 uniek	

Appendices to Chapter 7.5

Evidence tables

Table: Exclusion after re	evision of full text
Author and year	Reason for exclusion
Chang, 2013	Does not fulfill selection criteria
Choi, 2014	Does not fulfill selection criteria
Cruz, 2006	Does not fulfill selection criteria
Cruz, 2008	Does not fulfill selection criteria
Deray, 2006	Does not fulfill selection criteria
Frank, 2003	Already included in systematic review Cruz, 2012
Furukawa, 1996	Does not fulfill selection criteria
Gabutti, 2003	Does not fulfill selection criteria
Ghani, 2011	Does not fulfill selection criteria
Hsieh, 2005	Already included in systematic review Cruz, 2012
Huber, 2002	Does not fulfill selection criteria
Joannidis, 2010	Does not fulfill selection criteria
Lee, 2007	Already included in systematic review Cruz, 2012
Lehnert, 1998	Already included in systematic review Cruz, 2012
Marenzi, 2003	Already included in systematic review Cruz, 2012
Marenzi, 2004	Does not fulfill selection criteria
Marenzi, 2006	Already included in systematic review Cruz, 2012
Marenzi, 2007	Does not fulfill selection criteria
Moon, 1995	Does not fulfill selection criteria
Ono, 2004	Does not fulfill selection criteria
Reinecke, 2007	Already included in systematic review Cruz, 2012
Schindler, 2001	Does not fulfill selection criteria
Shinoda, 2002	Does not fulfill selection criteria
Song, 2010	Does not fulfill selection criteria
Song, 2011	Does not fulfill selection criteria
Sterner, 2000	Already included in systematic review Cruz, 2012
Vogt, 2001	Already included in systematic review Cruz, 2012

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/journal.pmed1000097)

Study	Appropriate and	Comprehensive	Description of	Description of	Appropriate adjustment for	Assessment of	Enough	Potential risk	Potential
	clearly focused	and systematic	included and	relevant	potential confounders in	scientific	similarities	of publication	conflicts of
	question? ¹	literature	excluded	characteristics	observational studies? ⁵	quality of	between studies	bias taken into	interest
		search? ²	studies? ³	of included		included	to make	account? ⁸	reported? ⁹
				studies? ⁴		studies? ⁶	combining them		
							reasonable? ⁷		
First author,									
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Cruz, 2012	Yes	Yes	No	Yes	No	Yes	Yes	No	No

10. Research question (PICO) and inclusion criteria should be appropriate and predefined

11. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched

12. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons

13. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported

14. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)

15. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)

16. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, 1²)?

17. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

18. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials) Research question:

Study	Describe	Bias due to	Bias due to loss to	Bias due to violation				
reference	method of	inadequate	inadequate	inadequate	inadequate	selective outcome	follow-up?⁵	of
	randomisation ¹	concealment of	blinding of	blinding of care	blinding of	reporting on basis		intention to treat
		allocation? ²	participants to	providers to	outcome assessors	of the results? ⁴		analysis? ⁶
			treatment	treatment	to treatment			
(first			allocation? ³	allocation? ³	allocation? ³			
author,								
publicatio		(unlikely/likely/un	(unlikely/likely/un	(unlikely/likely/uncl	(unlikely/likely/uncl	(unlikely/likely/uncl	(unlikely/likely/unclea	(unlikely/likely/uncle
n year)		clear)	clear)	ear)	ear)	ear)	r)	ar)
Spini,	Not randomised	Unlikely	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear
2013								

13. Randomisation: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.

14. Allocation concealment: refers to the protection (blinding) of the randomisation process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomisation (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomisation procedures or open allocation schedules..

15. Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignement influences the proces of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.

16. Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.

17. If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear

18. Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

Risk of bias table for intervention studies (observational: non-randomized clinical trials, cohort and case-control studies) Evidence table for systematic review of RCTs and observational studies (intervention studies) Research guestion:

Study	Study	Patient characteristics	Intervention (I)	Comparison /	Follow-up	Outcome measures and	Comments
reference	characteristics			control (C)		effect size	
Cruz,	SR and meta-	Inclusion criteria SR:	Describe	Describe control:	End-point of follow-	Outcome measure-1	Facultative:
2012	analysis of RCTs	1) studies that ecaluated the	intervention:		<u>up</u> :	Defined as RCIN	
	/ cohort studies	use of periprocedural renal		For all studies:		Reported for CKD stage 4-	Brief description of
individual		replacement therapy (RRT)	A: hemodialysis	Standard medical	Not reported	5 patients only	author's conclusion: In
study	Literature search	for the prevention of	(HD)	therapy, depending			this updated meta-
characteri	up to March	radiocontrast induced	B: HD	on hospital either		Effect measure: RR [95%	analysis periproceural
stics	2011	nephropathy (RCIN) as	C: HD	pre-hydration or	For how many	CI]:	RRT did not decrease the
deduced		compared with standard	D: HD	pre- and	participants were no	J: 3.43 (0.45 – 25.93)	incidence of RCIN
from [1st	A : Lee, 2007	medical treatment (SMT)	E: HD	posthydration	complete outcome	G: 1.56 (0.66 – 3.72)	compared with SMT. HD
author,	B: Reinecke,	2) 10 or more human	F: HD		data available?	D : 0.33 (0.01 – 7.72)	appears to actually
year of	2007	subjects	G: HD		Not reported	E: 0.12 (0.05 – 0.32)	increase RCIN risk.
publicatio	C: Marenzi, 2006	primary outcome: RCIN	H: HD			C: 0.48 (0.27 – 0.88)	
n	D : Hsieh, 2005	(sCR ≥0.5mg/dL / 44	I: Hemofiltration			I: 1.70 (0.59 – 4.90)	Personal remarks on
	E: Marenzi, 2003	umol/L); secondary	(HF)			H: 1.27 (0.80 – 2.01)	study quality,
	F : Frank, 2003	outcomes: need for	J: HF				conclusions, and other
PS., study	G : Gabutti, 2003	temporary acute RRT, need	K: Hemodiafiltration			Pooled effect (random	issues (potentially)
characteri	H : Vogt <i>,</i> 2001	for permanent RRT, long-				effects model):	relevant to the research
stics and	I: Sterner, 2000	term changes in renal				0.81 [95% Cl 0.37 to 1.76]	question:
results	J: Berger, 2001	function, death				favoring RRT.	In our own literature
are	K: Lehnert, 2008					Heterogeneity (I ²): 79%	analysis the observational
extracted		Exclusion criteria SR:					studies were excluded
from the	Study design:					Outcome measure-2	from the systematic
SR (unless	A: Randomized	11 studies included				Risk for acute RRT	review and only the RCTs
stated	trial						with patients CKD stage
otherwise	B: Randomized					HDF/HF	4-5 were included.
)	trial	Important patient				G: 2.89 (0.12 – 67.75)	
	C: Randomized	characteristics at baseline:				E: 0.14 (0.03 – 0.58)	Level of evidence: GRADE
	trial	Number of patients;				C: 0.16 (0.05 – 0.55)	Low to Very low for most
	D: Observational	characteristics important to				Pooled effect (random	studies due to high risk of
	E: Randomized	the research question and/or				effects model):	bias in several studies,
	trial	for statistical adjustment				0.22 [95% CI 0.06 to 0.74]	wide confidence intervals
	F: Randomized	(confounding in cohort				favoring RRT.	(imprecision) and

trial	studies); for example, age,		Heterogeneity (I ²): 36%	heterogeneity of included
G: Observational	sex, bmi,			studies
H: Randomized			HD	
trial	Number of patients, age		A: 0.07 (0.01 – 0.49)	
I: Randomized	(years)		B: 2.05 (0.29 – 14.41)	
trial	A : 82; 65-66		H: 2.81 (0.70 – 10.06)	
J: Randomized	B : 424; 67-68		Pooled effect (random	
trial	C : 92; 71-72		effects model):	
K: Randomized	D : 40; 66-69		0.78 [95% CI 0.07 to 8.43]	
trial	E : 114; 69		favoring RRT.	
	F : 17; 58-67		Heterogeneity (I ²): 83%	
	G : 49; 70			
Setting and	H : 113; 69-70			
<u>Country</u> : Italy	I:32; 65-72		Outcome measure-3	
	J: 15; 62-68		Risk for chronic RRT	
Source of	K: 30; 60-63			
funding:			HDF/HF	
No funding	<u>Sex</u> : not reported		E: 0.32 (0.03 – 3.00)	
	Groups comparable at		HD	
	baseline?		F: 1.43 (0.26 – 7.86)	
	Unclear		D: 1.33 (0.34 – 5.21)	
			A: 0.09 (0.00 – 1.52)	
			H: 2.11 (0.20 – 22.61)	
			Pooled effect (random	
			effects model):	
			0.87 [95% CI 0.33 to 2.29]	
			favoring RRT.	
			Heterogeneity (I ²): 19%	
			Outcome measure-4	
			Mortality	
			Not reported per study.	
			Pooled analysis for 5	
			studies.	
			I: 2.6%	

			C: 3.7%	
			RR: 0.65, 95% CI: 0.17 –	
			2.49	

CIN: contrast induced nephropathy; NAC: N-acetyl-cysteine; NR: not reported

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])¹ This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question:

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C) ³	Follow-up	Outcome measures and effect size ⁴	Comments
reference		2					
Spini,	Type of study:	Inclusion	Describe intervention	Describe control	Length of follow-up:	Outcome measures and	A limitation of using PC-
2013	prospective	<u>criteria</u> :	(treatment/procedure/test):	(treatment/procedure/test):	Creatinine levels – 72	effect size (include	AKI / CIN as an
	controlled	patients			hours	95%CI and p-value if	endpoint, is that
	trial	admitted to			Mortality 12 months, 18	available):	creatinine, which forms
		the cardiac	Continuous renal	CRRT only after	months		the base of the PC-AKI
	Setting:	stepdown at	replacement therapy (CRRT)	percutaneous intervention		Contrast induced	definition, is removed
	cardiac	the	at least 6 hours before and		Loss-to-follow-up: not	nephropathy (CIN):	by RRT. However,
	stepdown	participating	24 hours after contrast		reported	I: 0/25 (0%)	creatinine is removed by
		hospital	medium administration			C: 13/21 (62%)	CRRT.
	Country: Italy	-eGFR			Incomplete outcome	p-value not reported	
		<30mL/min			<u>data</u> :		
	Source of	-needed to be			Not reported	Worsening renal failure:	
	funding: not	submitted to				I: 3/25 (12%)	
	reported	percutaneous				C: 9/25 (43%)	
		intervention				p-0.042	
		Exclusion				Dialysis:	
		criteria: -				I: 2/25 (8%)	
						C: 9/21 (19%)	
		<u>N total at</u>				P=0.50	
		baseline: 46					
		Intervention:				Long-term mortality:	
		25				I: 4/25 (16%)	
		Control: 21				I: 12/21 (57%)	

		P0.009	
Important	<u>nt</u>		
prognostic	ic	Cardiovascular deaths:	
factors ² :		I: 0/25 (0%)	
For examp	ple	C: 5/21 (24%)	
age ± SD:	:	p-value not reported	
l: 73 ± 11			
C: 74 ± 8			
Sex:			
I: 84% M			
C: 67% M	1		
Groups			
comparab	ble at		
baseline?			

Notes:

5. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures

6. Provide data per treatment group on the most important prognostic factors [(potential) confounders]

7. For case-control studies, provide sufficient detail on the procedure used to match cases and controls

8. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Search description

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab.	194
(OVID)	(113850) 2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
1995- okt. 2015	(543550) 3 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9272)	
English	4 1 and 2 (9076) 5 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or cin or ciaki).ti,ab. (9272)	
	6 4 or 5 (16764) 7 exp Hemofiltration/ or exp Renal Dialysis/ (103123) 8 (Hemofiltrat* or Haemofiltrat* or Haemodiafiltrat* or Hemodiafiltrat* or Dialysis	
	or hemodialysis or haemodialysis).ti,ab. (130690) 9 7 or 8 (153364) 10 6 and 9 (918)	
	11 (prophyla* or prevent*).ti,ab. or pc.fs. (1907859) 12 10 and 11 (356)	
	13 limit 12 to (english language and yr="1995 -Current") (302) 14 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychlit or psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or	
	((selection criteria or data extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not humans/)) (254827) 15 13 and 14 (59)	
	16 (exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or	
	randomized controlled trial or multicenter study or clinical trial).mp. or comparative study.pt. or random*.ti,ab. or (clinic* adj trial*).tw. or ((singl* or doubl* or treb* or tripl*) adj (blind\$3 or mask\$3)).tw. or Placebos/ or placebo*.tw.) not (animals/ not humans/) [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (2605774)	
	17 13 and 16 (149) 18 The prevention of radiocontrast-agent-induced nephropathy by hemofiltration.m_titl. (1)	
	19 Effects of two different treatments with continuous renal replacement therapy in patients with chronic renal dysfunction submitted to coronary invasive procedures.m_titl. (1) 20 "Renal replacement therapies for prevention of radiocontrast-induced	
	nephropathy: a systematic review.".m_titl. (1) 21 18 or 19 or 20 (3) 22 15 or 17 (166)	
	23 21 and 22 (3) 24 17 not 15 (107) 25 remove duplicates from 15 (56)	
Embase	26 remove duplicates from 24 (104) 'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR 'kidney injury' OR aki OR nephrotoxicity)):ab,ti OR ciaki:ab,ti OR	
(Elsevier)	('contrast medium'/exp OR (contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR failure*)):ab,ti)) AND	
	[english]/lim AND [1995-2015]/py AND ('hemofiltration'/exp/mj OR 'hemodialysis'/exp/mj OR hemofiltrat*:ab,ti OR haemofiltrat*:ab,ti OR haemodiafiltrat*:ab,ti OR hemodiafiltrat*:ab,ti OR hemodialysis:ab,ti OR haemodialysis:ab,ti) AND ('prophylaxis'/exp OR prophyla*:ab,ti OR prevent*:ab,ti	
	OR prevention:Ink) 'meta analysis'/de OR cochrane:ab OR embase:ab OR psychlit:ab OR cinahl:ab OR medline:ab OP (systematic NEAP (1 (system OP overview)):ab ti OP (meta NEAP (1	
	medline:ab OR (systematic NEAR/1 (review OR overview)):ab,ti OR (meta NEAR/1 analy*):ab,ti OR metaanalys*:ab,ti OR 'data extraction':ab OR cochrane:jt OR 'systematic review'/de NOT ('animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp NOT 'human'/exp)) (26) – 9 uniek	
	AND ('clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo*:ab,ti) NOT 'conference abstract':it - (57) – 25 uniek	

Appendices to Chapter 8

Evidence tables

Table: Exclusion of article after examination of full tekst.

Table: Exclusion of article after o							
Author and year	Reason for exclusion						
Aronson, 2007 Baarlashar, 2012	Does not meet selection criteria						
Baerlocher, 2013	Review, not systematic						
Blickle, 2007	Does not meet selection criteria						
Bloomgarten, 1996	Does not meet selection criteria						
Boscheri, 2007	Does not meet selection criteria						
Chan, 1999	Does not meet selection criteria						
Chong, 2004	Does not meet selection criteria						
Cicero, 2012	Does not meet selection criteria						
Dawson, 2002	Does not meet selection criteria						
Dichtwald, 2011	Case series, no control group						
Douros, 2015	Does not meet selection criteria						
Elder, 2003	Does not meet selection criteria						
Erley, 2006	Does not meet selection criteria						
Goergen, 2010_1	Does not meet selection criteria						
Gomez-Herrerp, 2013	Does not meet selection criteria						
Gupta, 2002	Does not meet selection criteria						
Hammond	Does not meet selection criteria						
Heikkinen, 2007	Does not meet selection criteria						
Heupler, 1998	Does not meet selection criteria						
Hoste, 2013	Does not meet selection criteria						
Jain, 2008	Included in systematic review Goergen, 2010						
Jones, 2003	Does not meet selection criteria						
Kdogi, 2007	Does not meet selection criteria						
Khurana, 2010_1	Review, not systematic						
Khurana, 2010 2	Letter to editor						
Klepser, 1997	Does not meet selection criteria						
Koc, 2013	Does not meet selection criteria						
Lalau, 2001	Systematic review, however more recent systematic (Georgen, 2010) present						
, ,	and included in literature summary						
Landewe-Cleuren, 2000	Review, not systematic						
Leow, 2015	Does not meet selection criteria						
Longeran, 2008	Does not meet selection criteria						
McCartney, 1999	Systematic review, however more recent systematic (Georgen, 2010) present						
···· · · · · · · · · · · · · · · · · ·	and included in literature summary						
Millican, 2004	Does not meet selection criteria						
Morcos. 2001	Does not meet selection criteria						
Morcos, 2005	Does not meet selection criteria						
Nawaz, 1998	Included in systematic review Goergen, 2010						
Nolan, 1997	Does not meet selection criteria						
Parra, 2004	No control group.						
Pond, 1996	Does not meet selection criteria						
Quasny, 1997	Does not meet selection criteria						
Radwan, 2011	Does not meet selection criteria						
Rakovac, 2005	Does not meet selection criteria						
Rasuli, 1998_1	Does not meet selection criteria						
Rasuli, 1998_2	Does not meet selection criteria						
Safadi, 1996	Does not meet selection criteria						
Sayer, 2006	Letter to the editor						
Schweiger, 2007	Does not meet selection criteria						
Senior, 2012	Does not meet selection criteria						
Setter, 2003	Does not meet selection criteria						
Stacul, 2006	Does not meet selection criteria						
Stacul, 2006 Stacul, 2011	Guideline tekst, not an original article						

Thompson, 2000	Does not meet selection criteria				
Thomsen, 2003	Guideline tekst, not an original article				
Thomsen, 2010	Does not meet selection criteria				
Thomson 2010	Does not meet selection criteria				
Tonolini, 2012	Does not meet selection criteria				
Tzakias, 2013	Does not meet selection criteria				
Tzakias, 2014	Does not meet selection criteria				
Van Dijk, 2008	Does not meet selection criteria				
Widmark, 2007	Does not meet selection criteria				

Table of quality assessment for systematic reviews of RCTs and observational studies

Based on AMSTAR checklist (Shea et al.; 2007, BMC Methodol 7: 10; doi:10.1186/1471-2288-7-10) and PRISMA checklist (Moher et al 2009, PLoS Med 6: e1000097; doi:10.1371/iournal.pmed1000097)

	clearly focused question? ¹	and systematic literature	included and excluded	Description of relevant characteristics of included studies? ⁴	Appropriate adjustment for potential confounders in observational studies? ⁵	Assessment of scientific quality of included studies? ⁶	Enough similarities between studies to make combining them reasonable? ⁷	Potential risk of publication bias taken into account? ⁸	Potential conflicts of interest reported? ⁹
year	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear/notapplicable	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear	Yes/no/unclear
Goergen, 2010	Yes	Yes	Yes	Yes	Not applicable	Yes	Yes	No	No

1. Research question (PICO) and inclusion criteria should be appropriate and predefined

2. Search period and strategy should be described; at least Medline searched; for pharmacological questions at least Medline + EMBASE searched

3. Potentially relevant studies that are excluded at final selection (after reading the full text) should be referenced with reasons

4. Characteristics of individual studies relevant to research question (PICO), including potential confounders, should be reported

5. Results should be adequately controlled for potential confounders by multivariate analysis (not applicable for RCTs)

6. Quality of individual studies should be assessed using a quality scoring tool or checklist (Jadad score, Newcastle-Ottawa scale, risk of bias table etc.)

7. Clinical and statistical heterogeneity should be assessed; clinical: enough similarities in patient characteristics, intervention and definition of outcome measure to allow pooling? For pooled data: assessment of statistical heterogeneity using appropriate statistical tests (e.g. Chi-square, I2)?

8. An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). Note: If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.

9. Sources of support (including commercial co-authorship) should be reported in both the systematic review and the included studies. Note: To get a "yes," source of funding or support must be indicated for the systematic review AND for each of the included studies.

Risk of bias table for intervention studies (randomized controlled trials)

Evidence table for systematic review of RCTs and observational studies (intervention studies)

Research question:

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Goergen,	SR and meta-	Inclusion criteria SR:	Describe	Describe	End-point of follow-	Outcome measure-1	Facultative:
2010	analysis of [RCTs	1) English language publication	intervention:	control:	<u>up</u> :	Defined as presence of	

	/ cohort / case-	2) administration of iodinated				metformin associated	Brief description of
[individua	control studies]	contrast medium in adult	A: metformin and	A: not	A: not reported	lactic acidosis (MALA), or	author's conclusion:
l study	-	patients who were tacing	undergoing	applicable	B: not reported	relation between MALA	It is not clear whether
characteri	Literature search	metformin	angiography	B: not	C: not reported	and iodinated contrast	cessation of metformin in
stics	up to March	3) lactic acidosis was outcome	B: patients who had	applicable	D: not reported	medium administration	patient undergoing
deduced	2009	measure	metformin-	C : not applicable			intravascular contrast
from [1st			associated lactic	D: not		Effect measure: RR, RD,	administration for
author,	A : Nawaz, 1998	Exclusion criteria SR:	acidosis after use of	applicable	For how many	mean difference [95% CI]:	radiological examination
year of	B: MacCartney,	1) studies in children (<18	intravenous		participants were no	A: 4 patients died (2	is effective for decreasing
publicatio	1999	years)	iodinated contrast		complete outcome	attributed to acute renal	the risk of lactic acidosis
n]	C : Stades, 2004	2) procedures in which	medium		data available?	failure and lactic	and hyperglycemia.
	D : Jain, 2008	administration of contrast	C: patients who had		(intervention/control)	acidosis), in 29 patients	
PS., study		medium was not used	metformin-		A: not reported	with normal renal	
characteri	Study design:	lactic acidosis was not one	associated lactic		B: not reported	function no change was	Level of evidence:
stics and	RCT [parallel /	of the outcomes assessed	acidosis, 26% of		C: not reported	observed after procedure	GRADE:
results	cross-over],	publications that were	them received		D: not reported	B : in 16-17 out of 18	All included studies had a
are	cohort	letters, narratives, editorials,	contrast medium			cases renal dysfunction or	very low quality of
extracted	[prospective /	reviews based on only expert	prior			other contra-indication	evidence (summaries of
from the	retrospective],	opinion, draft reports	D: metformin-			was present	case-reports, case-series,
SR (unless	case-series,		associated lactic			C: 25% of cases had	case-report)
stated	case-control	4 studies included	acidosis,			intravascular contrast	-no studies with control
otherwise	A: case-series					medium administered	group
)	B: summary of					D: metformin-associated	
	case-reports	Important patient				lactic acidosis, developed	For study C (stades, 2004)
	C: summary of	characteristics at baseline:				in patient with normal	contrast medium was
	case-reports					renal function	administered in 26% of
	D: case report	<u>N, mean age</u>					the cases.
		A: 33, not reported					
		B: 18, not reported				Pooled effect (random	
	Setting and	C : 47, not reported				effects model / fixed	
	<u>Country</u> :	D: 1, not reported				effects model):	
	Australia, in- and					No pooling was possible	
	outpatiennts	<u>Sex</u> :				due to heterogeneity of	
	c c	A: not reported				included studies	
	Source of	B: not reported					
	funding:	C: not reported					
	Not reported	D: not reported			1		

Impaired renal function: A; 4/33 (12%) B:16/18 (89%) (unclear if this is correct number) C: not reported D: 0/1 (0%)			
Groups comparable at baseline? Not applicable (no control group)			

Search description

Database	Search terms	Total
Medline	1 exp Contrast Media/ or ((contrast adj3 iodine) or (contrast adj3 medi*)).ti,ab. (111686)	202
(OVID)	2 exp Kidney Diseases/ or (((kidney or renal) adj2 (disease* or injur* or failure*)) or	
(/	nephropath* or (renal adj2 (insufficienc* or function* or disease* or failure*))).ti,ab.	
1005	(534205)	
1995-now	3 1 and 2 (8890)	
	4 (((contrast* or ci) adj2 (nephropath* or 'kidney injury' or aki or nephrotoxicity)) or	
English	ciaki).ti,ab. (1942)	
Dutch	5 (meta-analysis/ or meta-analysis as topic/ or (meta adj analy\$).tw. or ((systematic* or literature) adj2 review\$1).tw. or (systematic adj overview\$1).tw. or exp "Review Literature	
	as Topic"/ or cochrane.ab. or cochrane.jw. or embase.ab. or medline.ab. or (psychilt or	
	psyclit).ab. or (cinahl or cinhal).ab. or cancerlit.ab. or ((selection criteria or data	
	extraction).ab. and "review"/)) not (Comment/ or Editorial/ or Letter/ or (animals/ not	
	humans/)) (244003)	
	6 3 or 4 (9377)	
	7 limit 6 to (yr="1995 -Current" and (dutch or english)) (5451)	
	8 Metformin/ or (metformin* or glucophage).ti,ab. (12587)	
	9 7 and 8 (53) – 52 uniek	
	'contrast induced nephropathy'/exp/dm_pc OR ((contrast* OR ci) NEAR/2 (nephropath* OR	
	'kidney injury' OR aki OR nephrotoxicity):ab,ti OR ciaki:ab,ti OR ('contrast medium'/exp OR	
	(contrast NEAR/3 iodine):ab,ti OR (contrast NEAR/3 medi*):ab,ti AND ('kidney disease'/exp	
	OR 'kidney function'/exp OR (kidney NEAR/2 (disease* OR injur* OR failure*)):ab,ti OR	
	nephropath*:ab,ti OR (renal NEAR/2 (insufficienc* OR function* OR disease* OR	
	failure*)):ab,ti)) NOT 'conference abstract':it AND ([dutch]/lim OR [english]/lim) AND	
	[embase]/lim AND [1995-2015]/py	
	AND ('metformin'/exp OR metformin*:ab,ti OR glucophage:ab,ti)	
	(191) – 150 uniek	